Heredity (2010) 104, 237–238

www.nature.com/hdy

NEWS AND COMMENTARY

Population cage experiments with an insect endosymbiont

An insect-endosymbiont conundrum

HCJ Godfray

Heredity (2010) **104,** 237–238; doi:10.1038/hdy.2009.144; published online 28 October 2009

Research over the last 20 years has shown that a large fraction of insect species has intimate associations with symbiotic bacteria that often have major effects on their biology. Some symbionts are mutualists increasing their host's fitness, whereas in other cases the host obtains no benefit or even suffers from carrying the micro-organism. Bacteria that do not benefit their carriers need other tricks to spread themselves through the host population. A particularly subtle strategy is *cytoplasmic incompatibility* (CI), in which, through a mechanism that is described below, the bacteria spread not by benefiting their host but by reducing the fitness of non-carriers. Until recently a single type of bacterium, *Wolbachia*, was thought to spread by CI. In 2003, Molly Hunter's group at Tucson discovered a second, unrelated bacterium, *Cardinium*, which could do the same thing (Hunter *et al*., 2003). In this issue, Harris *et al*. (2009) provide a rare quantitative test of the theory of bacterial spread by CI. They find that *Cardinium* spreads more readily than theory predicts and explore why this might be so.

The manner in which CI works in *Wolbachia* (and presumably in *Cardinium*, about which less is known) is that infected males in some way modify their sperm so that they can be utilized only by females that also carry the bacteria (Werren, 1997). Despite intensive investigation (and the availability of several complete *Wolbachia* genome sequences), it is still not understood how this modification/rescue system works mechanistically, although it seems to have something to do with the decondensation of the paternal chromosomes in the zygote. Females carrying *Wolbachia* can therefore mate successfully with any male, whereas uninfected females will have lower fitness because, whenever they mate with an infected male, their eggs will remain unfertilized. *Wolbachia* spread is therefore an example of what has been called 'evolutionary spite'—carriers obtain a relative fitness advantage by harming non-carriers. Note that when *Wolbachia* is rare, and non-carriers mate only occasionally with infected males, their relative fitness disadvantage will be small and the bacterial infection will increase only slowly. But as *Wolbachia* increases in frequency, uninfected females will suffer progressively higher costs, and the fraction of infected individuals will accelerate until everyone carries it.

The argument as just stated assumes that carrying the CI bacteria has no fitness consequences for the host. In fact, there is plenty of evidence that carriage may be costly, and also that the prohibition on the use of modified sperm by uninfected females may not be absolute. In these circumstances, theory predicts that there is a threshold CI bacteria frequency that has to be exceeded before the infection begins its autocatalytic spread. We can calculate that threshold (denoted by p) by recognizing that at this unstable equilibrium the fitness of infected and uninfected females must be exactly the same. Let us assume that carrying *Wolbachia* reduces the host fitness from 1 to $(1-s_f)$. The fitness of uninfected females is reduced whenever they mate with an infected male (probability p) by an amount equal to the probability that they cannot use the modified sperm (denoted by s_h), giving $(1-ps_h)$. Putting $(1-s_f)=(1-ps_h)$ and solving for p gives the threshold, $p=s_f/s_h$.

Based on previous studies and new experiments, Harris *et al*. (2009) were able to estimate these parameters. The strength of CI was not as high as often observed in *Wolbachia*, and uninfected females lost only about two-thirds of their offspring ($s_h=0.62$) when mating with infected males. Carrying *Cardinium* reduced the fecundity by about a fifth ($s_f=0.18$). Our calculation suggests that the threshold frequency that the *Cardinium* must attain before it can begin to spread is $0.18/0.62=0.29$. Harris *et al*. (2009) actually did a more sophisticated calculation (Turelli and Hoffmann, 1991; Vavre *et al*., 2000), taking into account the rare loss of the symbiont during maternal transmission and the haplodiploid genetics of the host (a parasitoid hymenopteran with a bizarre life history, but that is another story), and predicted the threshold was somewhat higher at $\sim$0.33, averaged across the sexes.

To test this prediction, Harris *et al*. (2009) set up population cages for which the initial frequency of infection was 0.15, $\sim$0.33 and 0.55, respectively. They expected that in the first case *Cardinium* would definitely invade, in the last case it definitely would not, while the middle case could go either way. To their surprise, *Cardinium* invaded in all cases. Why?

This is the first study of the dynamics of *Cardinium*, but related work on *Wolbachia* offers some clues as to what might be happening. The effect of *Wolbachia* on host fitness parameters can depend very subtly on the conditions under which they are measured (Hoffmann *et al*., 1990), and may also be affected by the internal dynamics of the bacterial population within the host, especially as it influences bacterial densities. A statistical analysis of the data suggests that they are best explained by assuming weaker CI and less costs (or even benefits). Perhaps the conditions in the population cages (and possibly also in the field) were more propitious to the bacterium than those in the laboratory experiments used to estimate the parameters. Over the last few years a series of fascinating examples of how some insect endosymbionts provide benefits to their host have been discovered, and in many cases the benefits are realized only when the host faces an abiotic or biotic challenge. It is likely that we are still some way from fully understanding all of the complexities of the mutualistic interaction. It could also be that in the interval between measuring the parameters and performing the experiment the bacteria have evolved. One of the best-studied endosymbiont interactions in the field involves a strain of *Wolbachia* attacking *Drosophila simulans* in California. Weeks *et al*. (2007) have recently shown that over the 20 years that it has been studied, it has evolved to be less costly to its host.

Only further study will resolve these issues. A better understanding of insect–symbiont biology will require not only mechanistic explorations of how the two parties interact, but also more cage and field population experiments to explore their population and genetic dynamics. Harris *et al*.'s (2009) blend of theory and experiments is a fine example of how this should be done.

Professor HCJ Godfray is at the Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3PS, UK.

e-mail: charles.godfray@zoo.ox.ac.uk

Harris LR, Kelly SE, Hunter MS, Perlman SJ (2009). Population dynamics and rapid spread of Cardinium, a bacterial endosymbiont causing cytoplasmic incompatibility in Encarsia pergandiella (Hymenoptera: Aphelinidae). *Heredity* **104**: 239–246.

Hoffmann AA, Turelli M, Harshman LG (1990). Factors affecting the distribution of cytoplasmic incompatibility in Drosophila simulans. *Genetics* **126**: 933–948.

Hunter MS, Perlman SJ, Kelly SE (2003). A bacterial symbiont in the Bacteroidetes induces cytoplasmic incompatibility in the parasitoid wasp Encarsia pergandiella. *Proc R Soc London B Biol* **270**: 2185–2190.

Turelli M, Hoffmann AA (1991). Rapid spread of an inherited incompatibility factor in California Drosophila. *Nature* **353**: 440–442.

Vavre F, Fleury F, Varaldi J, Fouillet P, Bouletreau M (2000). Evidence for female mortality in Wolbachia-mediated cytoplasmic incompatibility in haplodiploid insects: epidemiologic and evolutionary consequences. *Evolution* **54**: 191–200.

Weeks AR, Turelli M, Harcombe WR, Reynolds KT, Hoffmann AA (2007). From parasite to mutualist: rapid evolution of Wolbachia in natural populations of Drosophila. *PLoS Biol* **5**: 997–1005.

Werren JH (1997). Biology of Wolbachia. *Annu Rev Entomol* **42**: 587–609.

Editor's suggested reading

Clark ME, Bailey-Jourdain C, Ferree PM, England SJ, Sullivan W, Windsor DM *et al.* (2008). Wolbachia modification of sperm does not always require residence within developing sperm. *Heredity* **101**: 420–428.

White JA, Kelly SE, Perlman SJ, Hunter MS (2009). Cytoplasmic incompatibility in the parasitic wasp Encarsia inaron: disentangling the roles of Cardinium and Wolbachia symbionts. *Heredity* **102**: 483–489.

Ros VID, Breeuwer JAJ (2009). The effects of, and interactions between, Cardinium and Wolbachia in the doubly infected spider mite Bryobia sarothamni. *Heredity* **102**: 413–422.

Echaubard P, Duron O, Agnew P, Sidobre C, Noël V, Weil M *et al.* (2009). Rapid evolution of Wolbachia density in insecticide resistant Culex pipiens. *Heredity* (e-pub ahead of print 5 August 2009).