NEW NBU SCIENTIST IN BEE HEALTH

A Passion for Insects

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In May 2016, I joined the National Bee Unit (NBU) as a senior scientist in bee health. I have always had an interest in all of the sciences, but I studied biology as the high school I went to disapproved of young ladies studying physics. I was taken out of class one day and it was explained to me that biology would be a more appropriate choice as physics is quite hard. I didn't have the nerve to argue at that age.

This turned out to be a blessing, as I later discovered a real passion for insects and I consider myself very fortunate to have such an exciting job studying these fascinating creatures. These days, when I'm not working, I'm rooting around in the vegetation with my camera looking for insects to photograph.

Ceratitis capitata (medfly) female (left), Anastrepha ludens (mexfly) female (right)

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Eventually thankful that her traditionally-minded school thought she would be better off studying biology than her first love of physics, Kirsty Stainton discovered a passion for insects and pollinators and is now researching honey bee viruses at the National Bee Unit.

Combating Fruit Flies

After my degree in zoology at the University of Reading, I went on to study for my DPhil at Oxford University in collaboration with a small start-up company called Oxitec Ltd, which specialises in using biotechnology techniques for controlling insect pests.

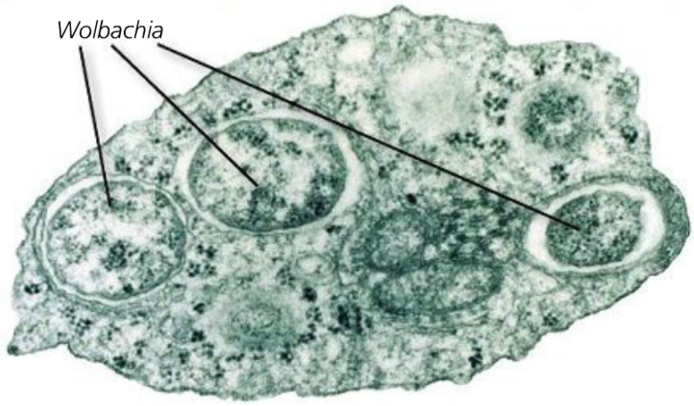
Oxitec is a spin-off company from Oxford University created by Luke Alphey, my PhD supervisor. During this time, I worked to develop genetically modified strains of the Mediterranean fruit fly (medfly), *Ceratitis capitata*, and the Mexican fruit fly (mexfly), *Anastrepha ludens*.

Both of these fruit fly species are found in South America and can cause massive agricultural losses by laying their eggs into fruit and coffee beans. Medfly is particularly damaging as it is such a generalist feeder and can attack hundreds of different crop plants.

Traditionally, these pests are controlled by use of the sterile insect technique (SIT), whereby irradiation-sterilised males are released into the field in their millions to seek out wild female mating partners. Females who mate with sterilised males will be unable to produce the offspring that eat their way through valuable fruit crops.

These programmes are very effective in eliminating pest populations as well as being species specific. This therefore reduces the need to apply insecticides. However, there is a costly inefficiency in the system: the facility that irradiates the males for release has to go to great effort to remove the females so that they are not released alongside the males. The strains which I helped to create eliminate females from populations of medfly[1] and mexfly[2].

I decided not to stay in the field of transgenic insect research; I was more interested in studying a mysterious bacterium found in insects.



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Transmission electron micrograph of Wolbachia *within an insect cell*

How Bacteria Can Manipulate Their Hosts

In 2008, I finished my PhD and began working as a post-doctoral researcher, again at Oxford University, studying an intracellular bacterium called *Wolbachia*. This is found in many species of insects: flies, bugs, beetles, butterflies, bees and wasps amongst many others. These bacteria manipulate their hosts on many levels.

Usually considered a reproductive parasite, *Wolbachia* has the ability to induce parthenogenesis (reproduction without fertilisation), male killing (all developing male embryos die) and cytoplasmic incompatibility (males infected with *Wolbachia* cannot fertilise eggs from uninfected females). This anti-male response means that *Wolbachia* can only be transmitted to the next generation by infected females, so it is in the interest of the bacterium to propagate itself by favouring infected females.

Nobody knows how *Wolbachia* causes these effects, but work with *Wolbachia*-infected insects found that the sperm from infected males cannot fertilise eggs from uninfected females.

After the sperm enters the egg, the unpackaging of the DNA from the sperm is disrupted and prevents the egg from developing into a viable embryo[3]. I have been involved in work where we tried to determine the genes that might be involved[4].

More recently, a colleague and I dissected sperm from flies for eight months (sperm are very small!) to see if we could identify any proteins in the sperm that might be involved (that research manuscript is in preparation).

Some strains of *Wolbachia* can make their hosts immune to viruses without damaging the host. I spent many years investigating how *Wolbachia* does this. Using a mosquito cell line created from the mosquito that transmits dengue virus (*Aedes aegypti*) and other viruses, I looked at how to reverse the viral suppression in *Wolbachia*-infected cells. Doing so would allow us to understand the mechanism that *Wolbachia* uses to make cells immune to viruses. If we can understand this, we may gain some insight into how to inhibit viruses.

In my final months working with *Wolbachia*, I discovered a compound that inhibits dengue virus in normal mosquito cells, but in *Wolbachia*-infected cells it reverses the viral resistance (manuscript in review). This work inspired me to inquire about how what I had learned might be useful in the study of honey bee viruses, having always had a passion for pollinators.

The Pull of Honey Bees

In 2012, I joined the Oxfordshire Beekeepers' Association and took a beginners' beekeeping course. I also went to the British Beekeepers' Association Spring Convention at Harper Adams University in Shropshire, where I was further inspired by Alan Bowman and his work on controlling varroa populations.

Later, when I read Stephen Martin's paper about varroa causing an increase in a more pathogenic form of deformed wing virus (DWV), I knew this was an idea I had to pursue[5].

Professor Martin's paper demonstrates that non-native organisms can drive a change in virus communities, causing them to become more virulent. There is evidence of *Wolbachia* in honey bee populations in the UK, but only an extremely low number of infected individuals have ever been detected, so whether it affects viruses is unknown.

At the moment, my colleague, Giles Budge, and I are studying chronic bee paralysis virus (CBPV) and DWV and we recently won a grant to study the effects of certain compounds on inhibition of these viruses. We will be using our compounds to see if we can suppress levels of virus in bees that we have artificially inoculated with CBPV or DWV.

We are expecting the preliminary results of this research project in summer 2017. I am really looking forward to meeting with beekeepers in the future and reporting on the progress of my research.

References

1 Fu, G, et al (2007). Female-specific insect lethality engineered using alternative splicing. *Nature Biotechnology*, **25**, 353–357.

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3 Serbus, LR, et al (2008). The genetics and cell biology of *Wolbachia*-host interactions. *Annual Review of Genetics*, **42**, 683–707. doi: 10.1146/annurev.genet.41.110306.130354

4 Pinto, SB, et al (2013). Transcriptional Regulation of *Culex pipiens* Mosquitoes by *Wolbachia* Influences Cytoplasmic Incompatibility. *PLoS Pathogens*, **9**(10), e1003647. doi: 10.1371/journal.ppat.1003647

5 Martin, SJ, et al, (2012). Global honey bee viral landscape altered by a parasitic mite. *Science*, **336**, 1304–1306. doi: 10.1126/science.1220941

Kirsty and her beloved Land Rover Defender