What are you focusing on at the moment? I am still carrying on with my research into the molecular mechanisms of memory, currently focusing on the link between CaMKII and AMPA receptors during memory consolidation. But two years ago, funded by the BBSRC, we embarked on an exciting new project, investigating the link between decision-making and learning in *Lymnaea*. This project uses much less molecular analysis than my previous projects, instead relying on some powerful new neurophysiological methods, such as multi-electrode array (MEA) recording and dynamic clamp as well as classical intracellular microelectrophysiology, a technique I first learned when I was still working on my PhD project in Hungary. The big scientific question we are focusing on at the moment is how such complex behavioural phenomena as decision-making are generated at the level of precisely defined and interacting neural networks and how they are shaped by learning.

What is your opinion concerning the future of invertebrate model systems in neuroscience research? Some years ago a certain 'gloom-and-doom' sentiment started spreading in the invertebrate neuroscience community concerning the future of the use of invertebrate model organisms in biomedical research. Undoubtedly, it is much harder to get neuroscience research on invertebrate animals funded than it was say 10 years ago. However, to a large extent this is also true for research using vertebrate models. I still believe that, at least in the UK, research based on exciting new ideas and using powerful new tools to address still unresolved questions of general biological importance still has a good chance of being funded, whatever the model system. I am convinced that research using invertebrates will continue to make a significant contribution to our understanding of the most fundamental and evolutionarily conserved principles of nervous system function and dysfunction.

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Quick guide

Entomopathogenic nematodes

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What are entomopathogenic nematodes? Nematodes seem to have evolved to occupy nearly every niche imaginable, including a wide diversity of parasitic niches. Among the vast variety of parasitic nematodes, some have evolved an association with insect-pathogenic bacteria. Together the bacteria and nematode are a lethal duo. These nematodes are called 'entomopathogenic nematodes'. Essentially the nematodes serve as mobile vectors for their insect-pathogenic bacteria cargo, like little Typhoid Marys. The nematodes seek out and invade potential hosts and release their pathogenic payload into the nutrient-rich hemolymph. Infected insect hosts die quickly, the bacteria proliferate, the nematodes feed on bacteria and insect tissues, and reproduce. When the host cadaver is depleted of resources, nematodes associated with pathogenic bacteria emerge and search for new hosts to infect (Figure 1). The cooperation with bacteria and the speed with which they kill set entomopathogenic nematodes apart from other nematode parasites.

How do they kill? The nematode and its pathogenic bacteria cargo contribute to varying degrees, depending on the specific combination. The known bacterial associates of entomopathogenic nematodes, *Photorhabdus* and *Xenorhabdus* species, are known to produce a toxic cocktail of secondary metabolites that not only are lethal to the insect hosts, but also prevent opportunistic bacteria and fungi from utilizing the nutrient-rich cadaver, sequestering the resources for themselves and their nematode partners. The bacteria always contribute to the virulence of the duo, and usually contribute the lion's share. Some species of nematodes are thought merely to shuttle the bacteria, contributing very little to host death, while others are known to be lethal in their own right, producing a variety of secreted protein products that degrade and digest host tissues, in addition to short-circuiting the host immune system. Even though some nematodes appear lethal on their own, all entomopathogenic nematodes known are associated with bacteria.

Are all stages infectious? The short answer is no. Only a modified third larval stage called the infective juvenile, analogous to the dauer juvenile stage in *Caenorhabditis elegans*, is infectious. In fact, infective juveniles are the only free-living stage of known entomopathogenic nematodes, while all other developmental stages are only found inside infected hosts. The infective juvenile is a stress-tolerant, non-feeding, bacterial-vectoring stage that seeks out insects to infect and kill.

How did they get their name? The first entomopathogenic nematode was described by Gotthold Steiner in 1923; since then more than 75 species have been described, with more species being described every year. Most studies focus on entomopathogenic nematodes from two genera: *Steinernema* and *Heterorhabditis*. It is through their association with insect-pathogenic bacteria that they began to be called entomopathogenic nematodes. First the nematodes' bacterial partners were called entomopathogenic bacteria because these bacteria have a median lethal dose or LD_{50} of 10,000 cells or less. This means that an inoculum of 10,000 bacterial cells or less, into the hemolymph, kills half of a tested population of insects. The term 'entomopathogenic' began to be applied to the nematodes themselves in the late 1980s and reinforces the link between nematology and insect pathology. It is a useful technical epithet that differentiates them from other types of parasitic nematodes, of which there are many.

Are they harmful to humans? While most parasitic nematodes might be seen as harmful, entomopathogenic nematodes are beneficial to humans. Their potential as alternatives to chemical pesticides for controlling pesky insects was recognized early

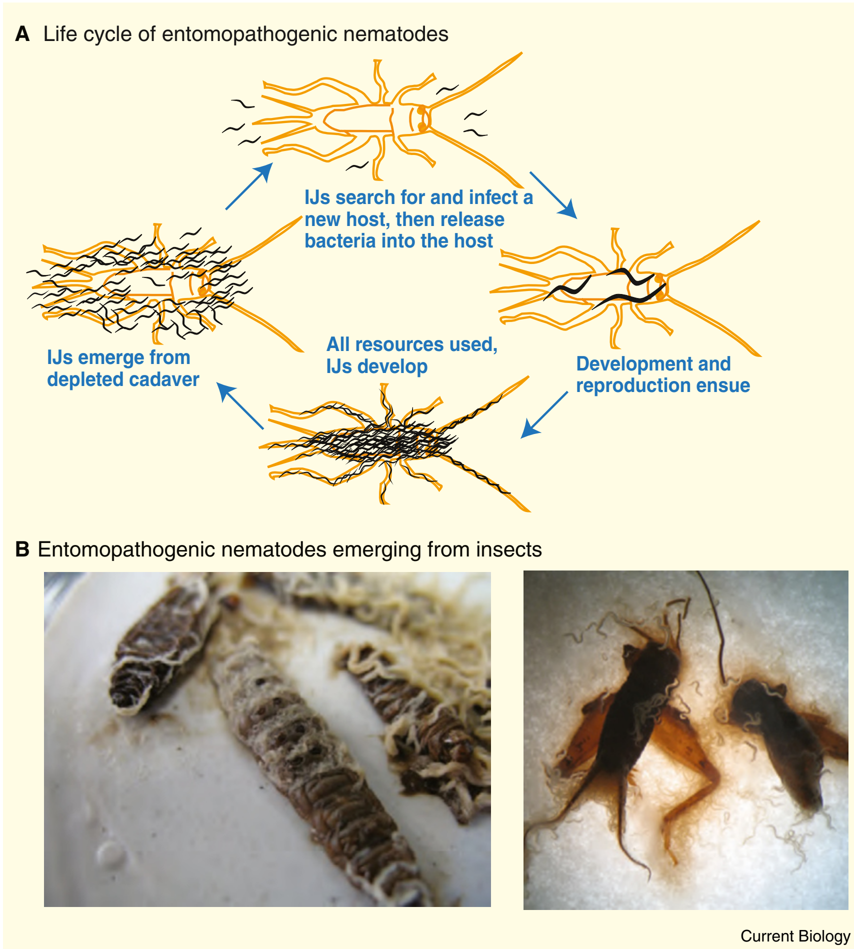

Figure 1. Life cycle of entomopathogenic nematodes.
(A) The infective juvenile (IJ) stage seeks out a new host to infect, penetrating into the hemolymph and releasing the pathogenic bacteria it carries. The nematodes develop and reproduce in the nutrient-rich insect, going through several rounds of reproduction, depending on the size of the insect host. As resources deplete, a new generation of infective juveniles form and emerge, seeking new hosts to infect with the pathogenic bacteria they carry. (B) Pictures showing entomopathogenic infective juveniles emerging from *Galleria mellonella* waxworm larvae on the left and *Acheta domestica* crickets on the right.

on and they have been subjected to extensive laboratory and field testing. Entomopathogenic nematodes have been used in biological control since the 1930s and are currently used worldwide. For example, they have been used with high levels of success to control invasive species of mole crickets in Florida and continue to be used in orange groves in both Florida and California to control the citrus root weevil and other damaging crop pests. Entomopathogenic nematodes are even commercially available for pest control in home gardens and are commonly marketed as 'beneficial nematodes.'

Why are entomopathogenic nematodes being studied? For starters, the symbiotic association with bacteria is highly specific in most cases and provides an excellent model for understanding the development and evolution of symbiosis. The potential of entomopathogenic nematodes to be used as biological-control agents continues to be evaluated with studies focusing on selection of desirable traits, such as virulence, heat and stress tolerance, and persistence. Because at least two distantly related genera have evolved this specific type of parasitism (*Heterorhabditis* and *Steinernema*), entomopathogenic nematodes are an interesting system for the study of convergent and parallel evolution. Also, since they are odd intermediates between predators and parasitoids, there are many studies regarding their host-seeking behavior. They rely primarily on chemoreception for host seeking and some of them are capable of jumping, which is an extraordinary behavior in nematodes that is unique to some *Steinernema*. Imagine, a 0.5–1 mm worm that has no legs or hard body parts yet is capable of jumping up to nine times its body length.

What remains to be explored? There is much that remains unknown about entomopathogenic nematodes, including: their global abundance and diversity; the extent of their host range and whether or not other arthropods or even non-arthropods are also infected; what has led to the specialization of some for certain hosts and not others; what drives niche partitioning within this guild; the molecular underpinnings of their symbiosis and parasitism; how they can survive carrying highly pathogenic bacteria; how they suppress or avoid host immunity; or just how genetically similar disparate species that have converged on this very particular lifestyle are. These and other questions remain underexplored, providing plenty of scope for studying these fascinating, useful, and delightful worms.

Where can I find out more?

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