Weird World of Parasites & Parasitic Mind Control of Host Behavior

CHARLIE VELLA, PHD, 2021

THANKS TO KARL ZIMMER, TRISTRAM WYATT

Amazing connections in Nature

- One night I was bored and started roaming the internet:
- What I came across:
- Parasitic wasps and caterpillars, which lead me to
- Role of coevolution and evolutionary arms races
- Red Queen hypothesis
- and then to plant sensory defense systems
- Also weird caterpillars

Weird Beauty:
Spicebush swallowtail: snake mimic

Puss moth caterpillar

Sonora Caterpillar: social

Hubbard's silkmoth caterpillar: 2.5 inches

American Daggermoth: toxic

Flannel moth: venomous spikes

Hickory Horned Devil: 5.9”
Royal Walnut Moth

Jewel caterpillar: half an inch

Jewel

Monkey Slug or Hagmoth caterpillar

Removable legs

Evolution is amazing

- While a 100-foot long blue whale or a brilliantly iridescent blue morpho butterfly are amazing products of evolution, the co-evolution of creatures that can mind control another creature into doing its bidding is also astounding.
- Natural world is an amazingly dangerous place.
- Evolutionary arms race for millions of years. Parasite virulence vs host immunity. Insect hosts react to parasites with their immune defenses. Parasites develop ways to thwart these defenses (i. e. genetic, viral, morphological, behavioral). Hosts respond in kind.
- There are trophic levels in food chain: plant, herbivore/caterpillar, parasite, hyperparasite, etc.

Assumptions we have can be challenged by parasites

- Animal’s behavior is under their own control.
- We have free will

Parasites

- A **parasitoid** is an organism that lives in close association with its host at the host's expense, eventually resulting in the death of the host.
- They are a fundamental part of ecosystems.
- They can have incredible complicated life cycles in many different hosts.
- But there is a cascade of brain controlling parasites that includes wasps, worms, viruses, fungi, and insects, that override the host’s behavioral control systems

Parasites

- Nearly every insect species has its own species of parasitoid wasp that specializes in murdering it.
- Many parasitic wasps have their own hyperparasite
- Great examples of coevolution and evolutionary arms races
- Because they eradicate "pest species", they are often used as biological pest control.
- Wonderful parasite life cycle graphics: DPDx - Laboratory Identification of Parasites of Public Health Concern

Parasite: Being a parasite is a really popular evolutionary option

- Estimates that 40% of animal species are parasitic
- Around 90 percent of parasitic animal species belong to just ten major groups, like wasps, flatworms, and nematode worms.
- These ten are all ancient; they took to parasitism during Cretaceous period (145-66 Ma); have been exploiting their fellow animals ever since.
- The arthropods—the hard-shelled, joint-legged group that includes insects, spiders, and crustaceans—have done so the most frequently
- Parasitism has evolved among animals at least 223 times

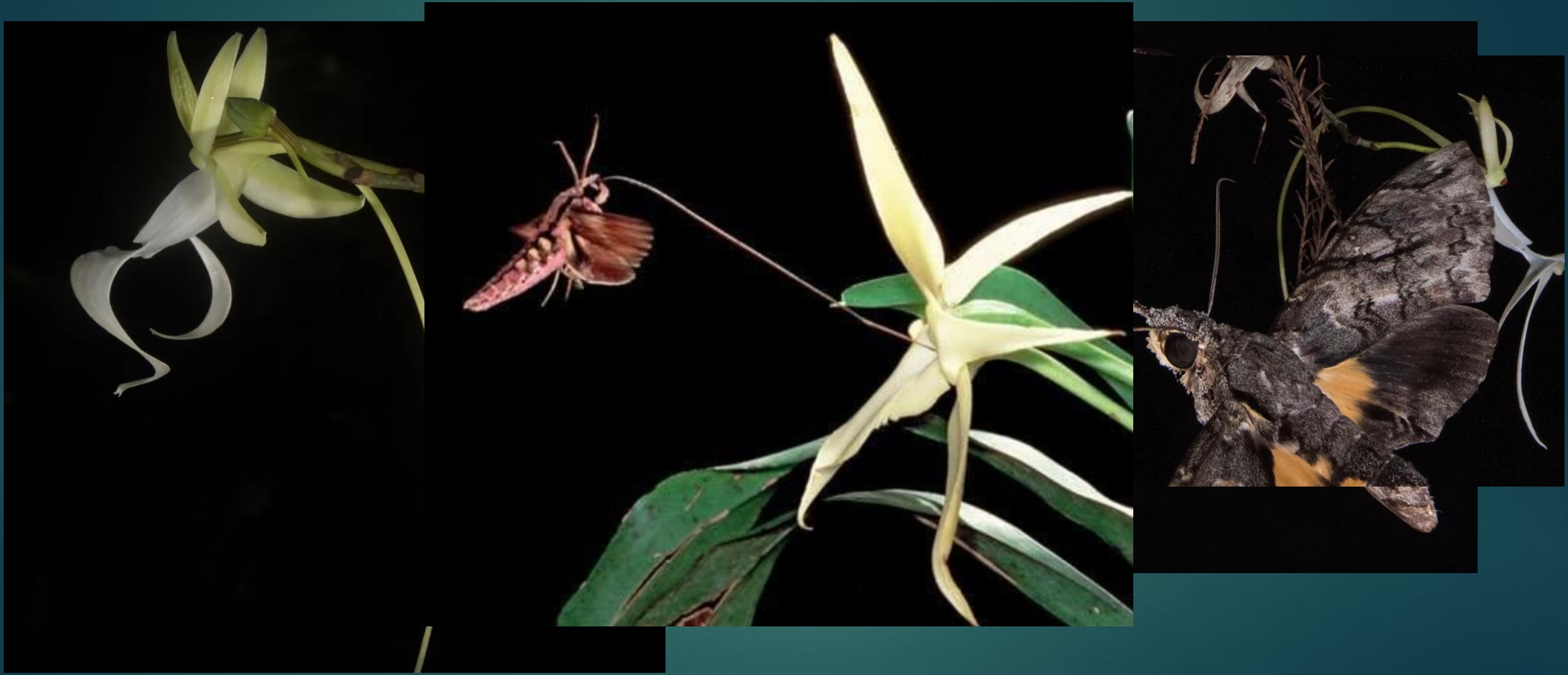
Independent origins of parasitism in Animalia -- Sara B. Weinstein and Armand M. Kuris, 2016

30 to 40 million years old Wasp inside a fly pupa

An x-ray of one of the fossilized parasites, showing the wasp visible inside a fly pupa.

Thomas van de Kamp

Coevolution: Darwin’s orchid: Malagasy star orchid

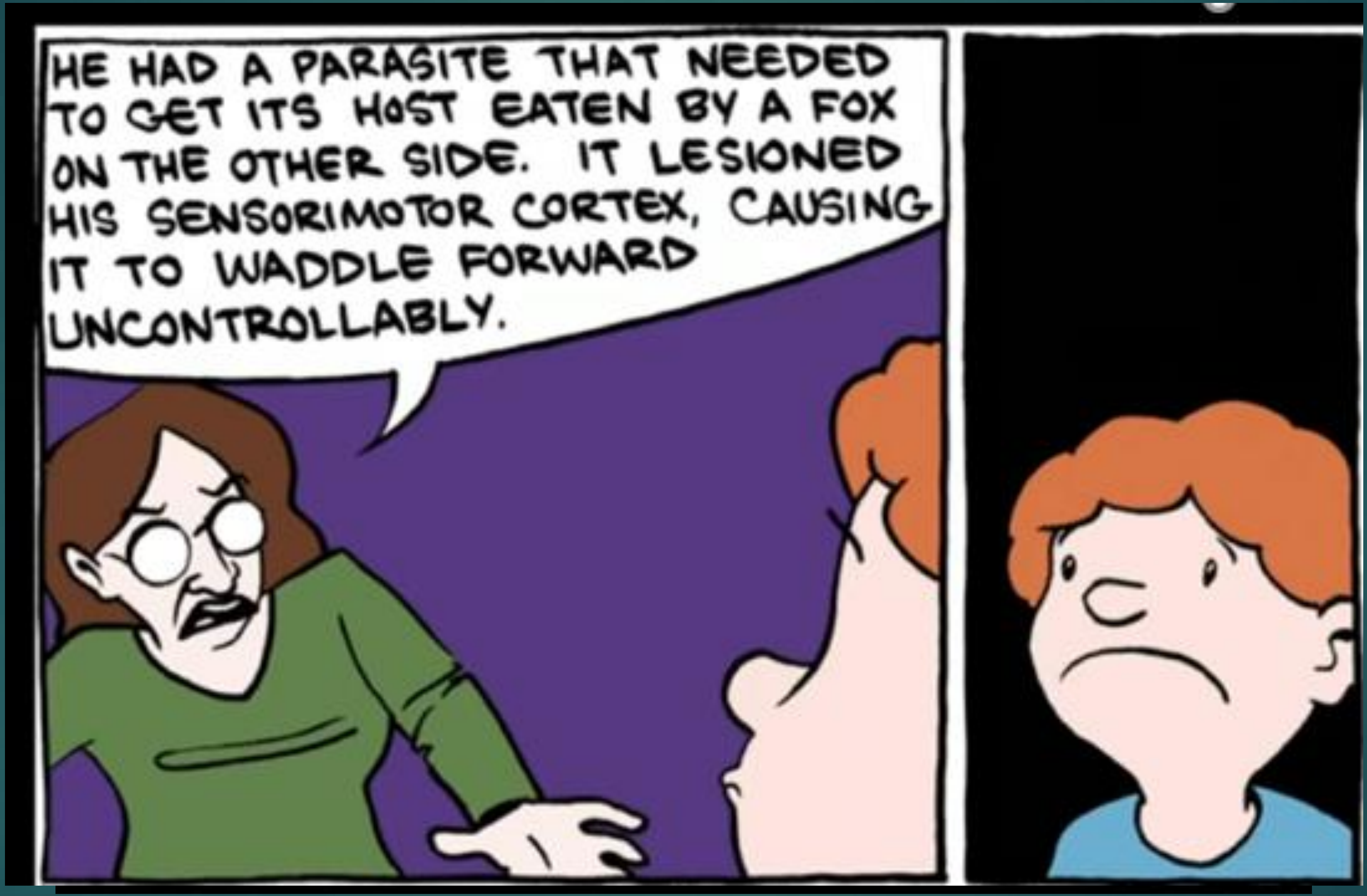


Darwin got orchid in 1861; moth not discovered until 1907: Darwin’s hawkmoth (*Xanthopan morganii praedicta*),

Not covered here: Parasites in Humans

- Tapeworms
- Hookworm/nematode
- Blood Flukes/flatworms
- Pinworms
- Roundworm/Nematode: Trichinosis
- Scabies mite
- Toxoplasma gondii
- Giardia lamblia

Parasites explain the frequent question



Chicken Parasites: Tapeworms, Roundworms, Threadworms

Jonathan Swift: "So, naturalists observe, a flea has smaller fleas that on him prey; and these have smaller still to bite ’em; and so proceed *ad infinitum."*

- A hyperparasitoid wasp (Pteromalidae) on the cocoons of its host, a braconid wasp (probably *Cotesia*) which is itself a parasitoid of a butterfly.

Darwin’s reaction to concept of Parasitic wasps…

Darwin, God, and Ichneumonidae (Parasitic wasps)

- The apparent cruelty of the ichneumonids troubled philosophers, naturalists, and theologians in the 19th century, who found the parasitoid lifestyle inconsistent with the notion of a world created by a loving and benevolent God.
- Parasitoid wasps are the subject of one of Charles Darwin's most famous quotations in 1860 in a letter to pioneering botanist Asa Gray:

The agnostic Darwin on parasitic wasps

- *“With respect to the theological view of the question: This is always painful to me. I am bewildered. I had no intention to write atheistically, but I own that I cannot see as plainly as others do, and as I should wish to do, evidence of design and beneficence on all sides of us. There seems to me too much misery in the world.*
- I cannot persuade myself that a beneficent and omnipotent God would have designedly created the Ichneumonidae with the express intention of their feeding within the living bodies of caterpillars, or that a cat should play with mice.”

Kind of wasps you know: build paper nest

Parasitic Wasps

- Wasps are the horror-film killers of the insect world. Sure, their stingers are scary, but it’s their parasitizing practices that really send a shiver down our skeleton.
- They are insects that eat other insects alive. They don’t just kill them, they want to keep them alive for as long as possible.
- Known as parasitoid wasps, these types of wasps are much smaller than the yellow jackets that make people panicky at picnics. With needlelike ovipositors, parasitoid wasps lay their eggs into or on top of other insects. As the young wasps grow, they devour their hosts and eventually kill them, sometimes by bursting through their abdomens like in the movie “Alien.”

Despite Darwin's disgust, God's favorite creature is…

- Quote by evolutionary biologist JBS Haldane that God has an "Inordinate Fondness For Beetles“ (350 K species), it is becoming apparent that God's chosen ones are Darwin's abhorred wasps

- Study: Hymenoptera (insect order that contains ants, bees and wasps) are the largest order of insects: 2 to 3 times as many hymenopterans as there are beetles: 1 M to 473 K species of Hymenoptera

- Most of the diversity within the hymenopterans are parasitic wasps, making them the most species-rich group of animal on this planet = 1 M to 400 K species. 1 study found 3 to 9 parasites for each insect species. There are parasites for each of their life stages (egg, larval and pupa).

- So rather than beetles, the animal group which the hypothetical Creator is most fond of appears to actually be body-snatching parasitic wasps

A. Forbes, et al., 2018

Art imitates life: The Alien films

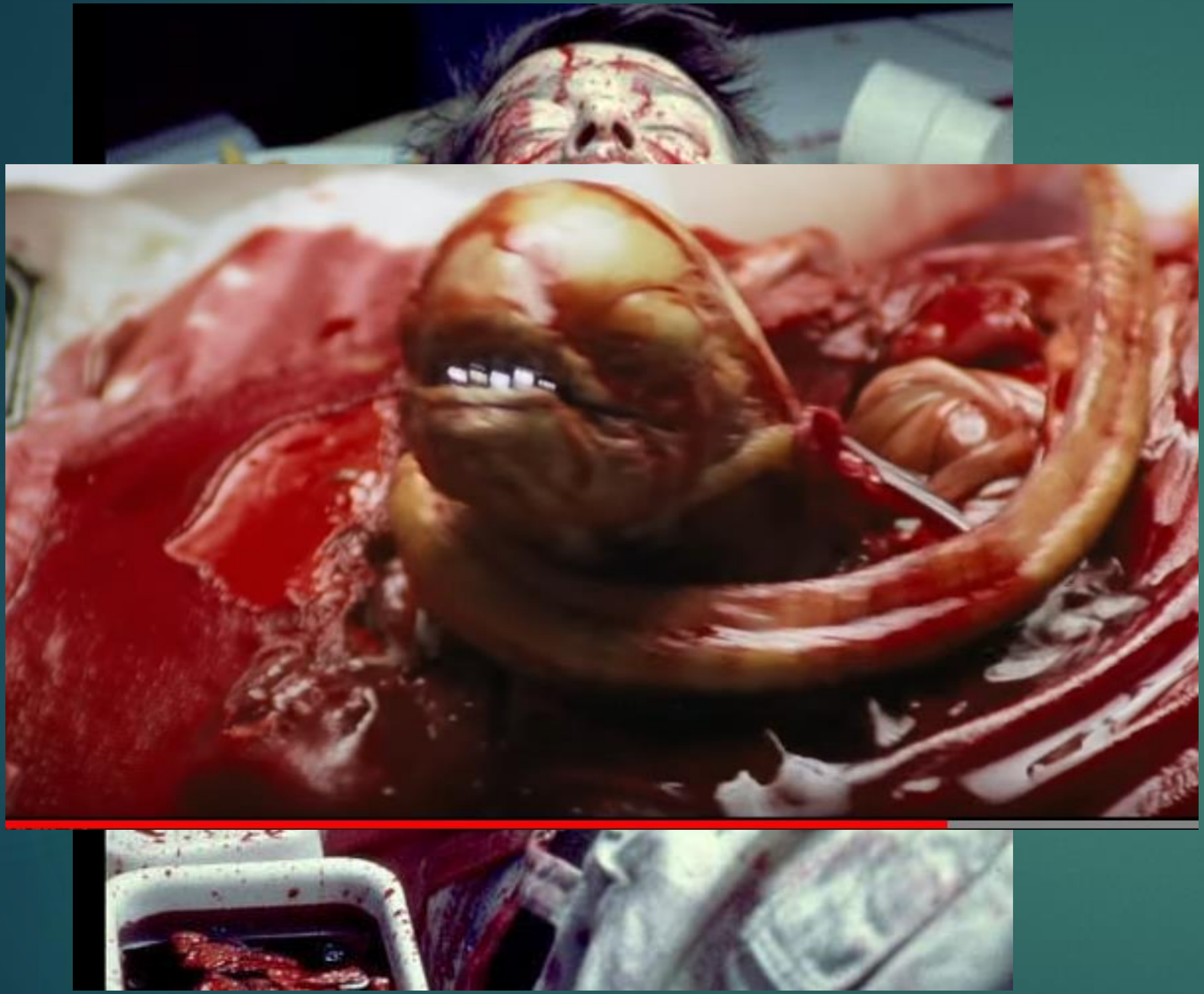
- The science fiction of the *Alien* film franchise is a famous example of art imitating life.
- These films present audiences with a terrifying monster with an unspeakably awful method of reproduction, which happens to closely resemble the lifecycles of scores of invertebrate parasite species on earth.

Complex Life cycle of Alien parasite

Egg

Ovipositor: implant larva

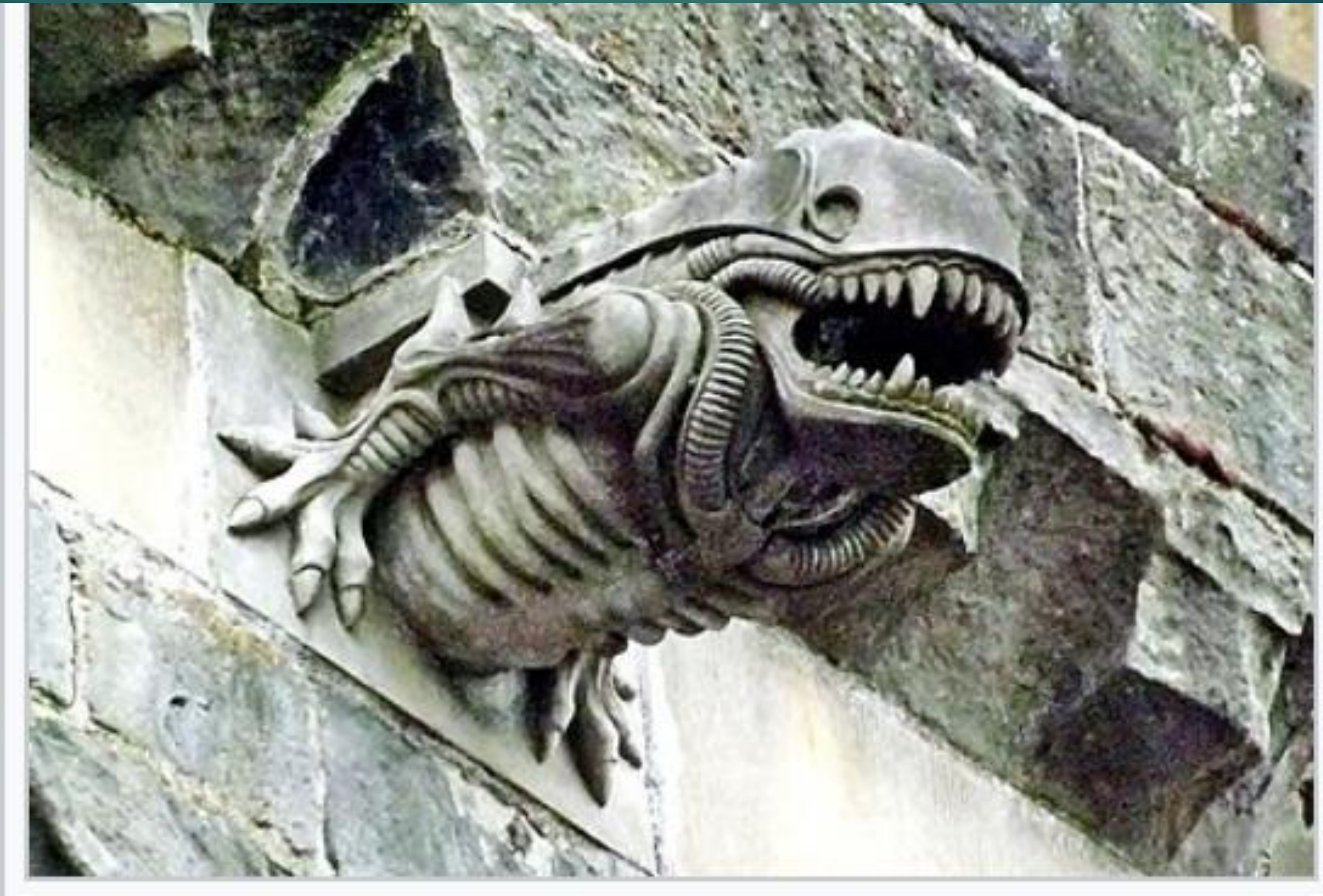
In the movies: USCSS Nostromo



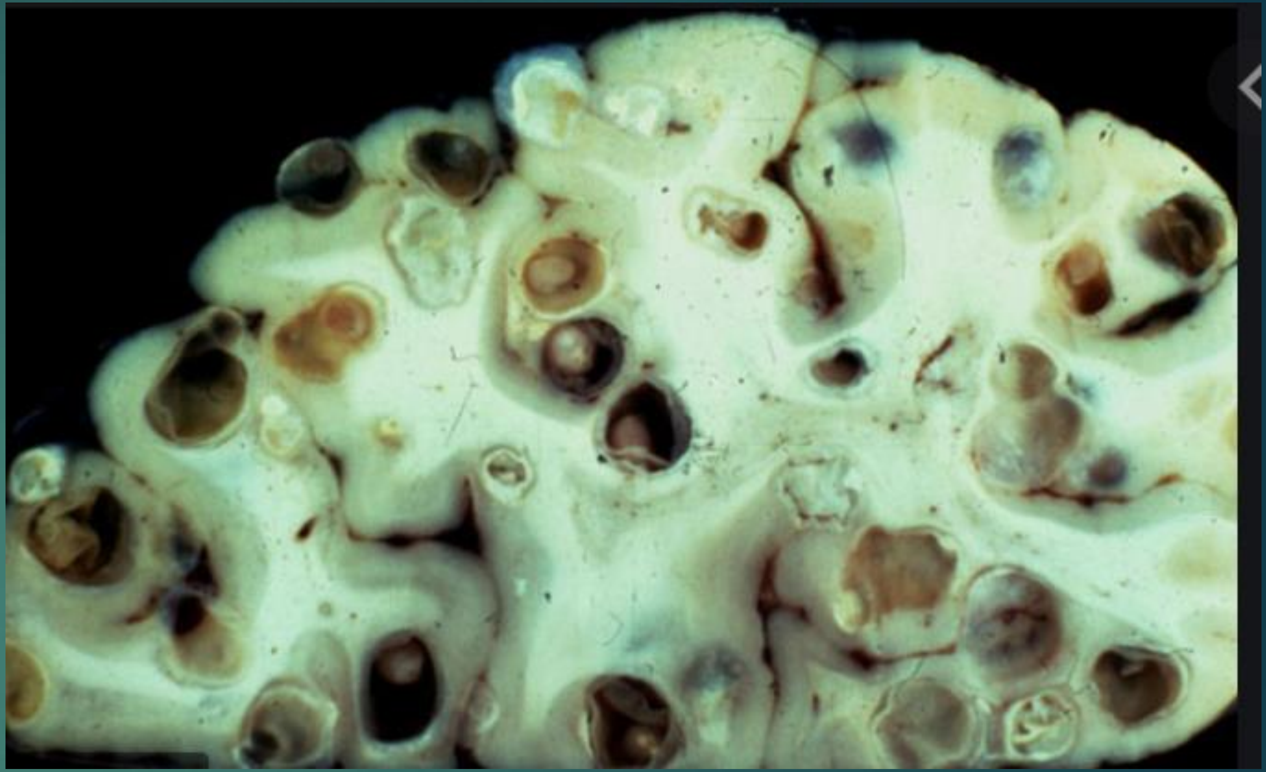
Larva emerges

Adult

A 1990s gargoyle at Paisley Abbey, Scotland, resembling a Xenomorph parasitoid from the film *Alien*



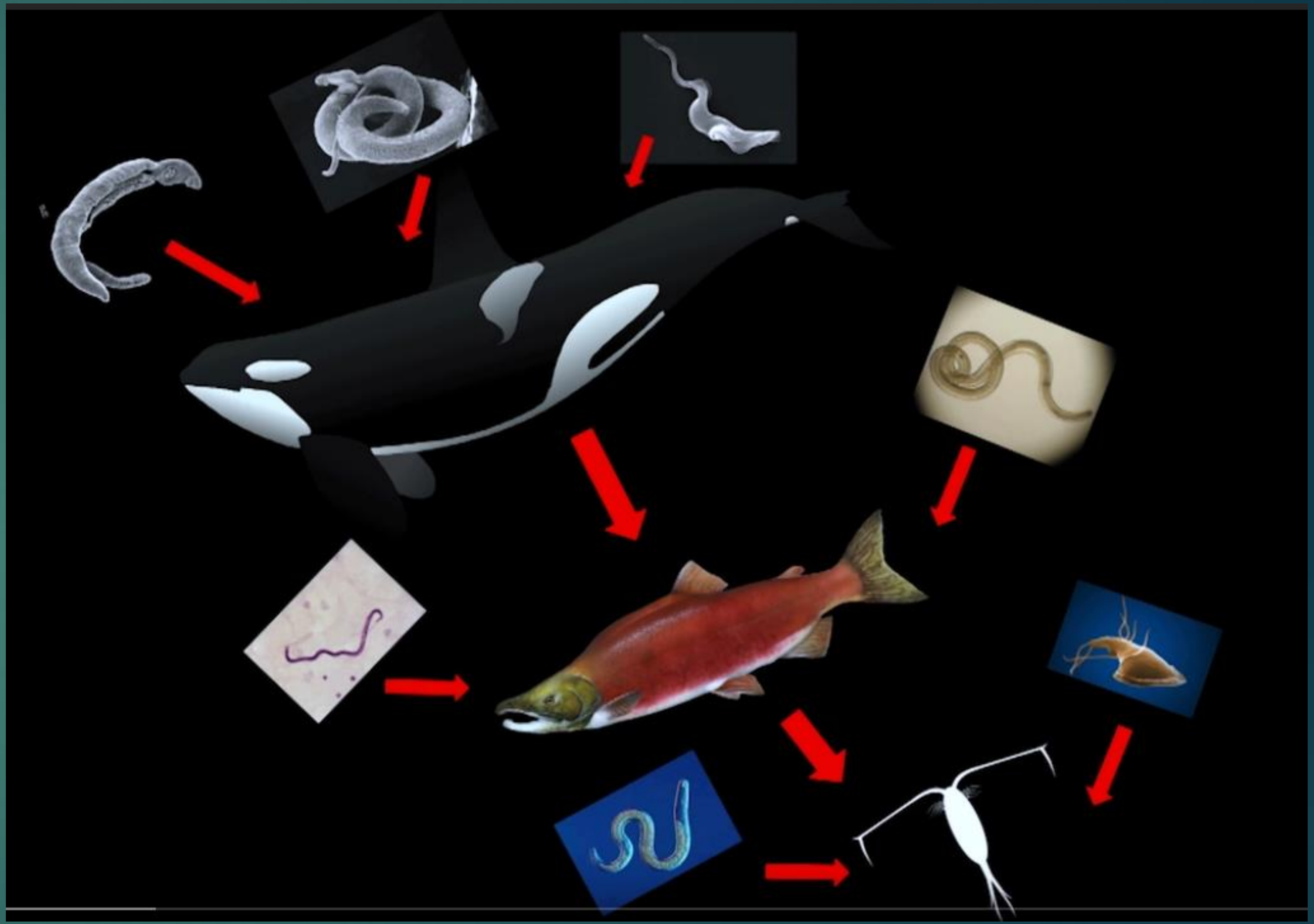
Parasites are everywhere and are often associated with sickness. We often have a disgust reaction.



Cysticercosis: A human brain overrun with cysts from Taenia solium, a tapeworm that normally inhabits the muscles of pigs.

Parasite basics: 1 - Multitude of Parasite species

- Ecologists think parasites are most common life form on earth
- Each part of ecological food chain level has its associated parasites



Parasites: Horror & Fascination

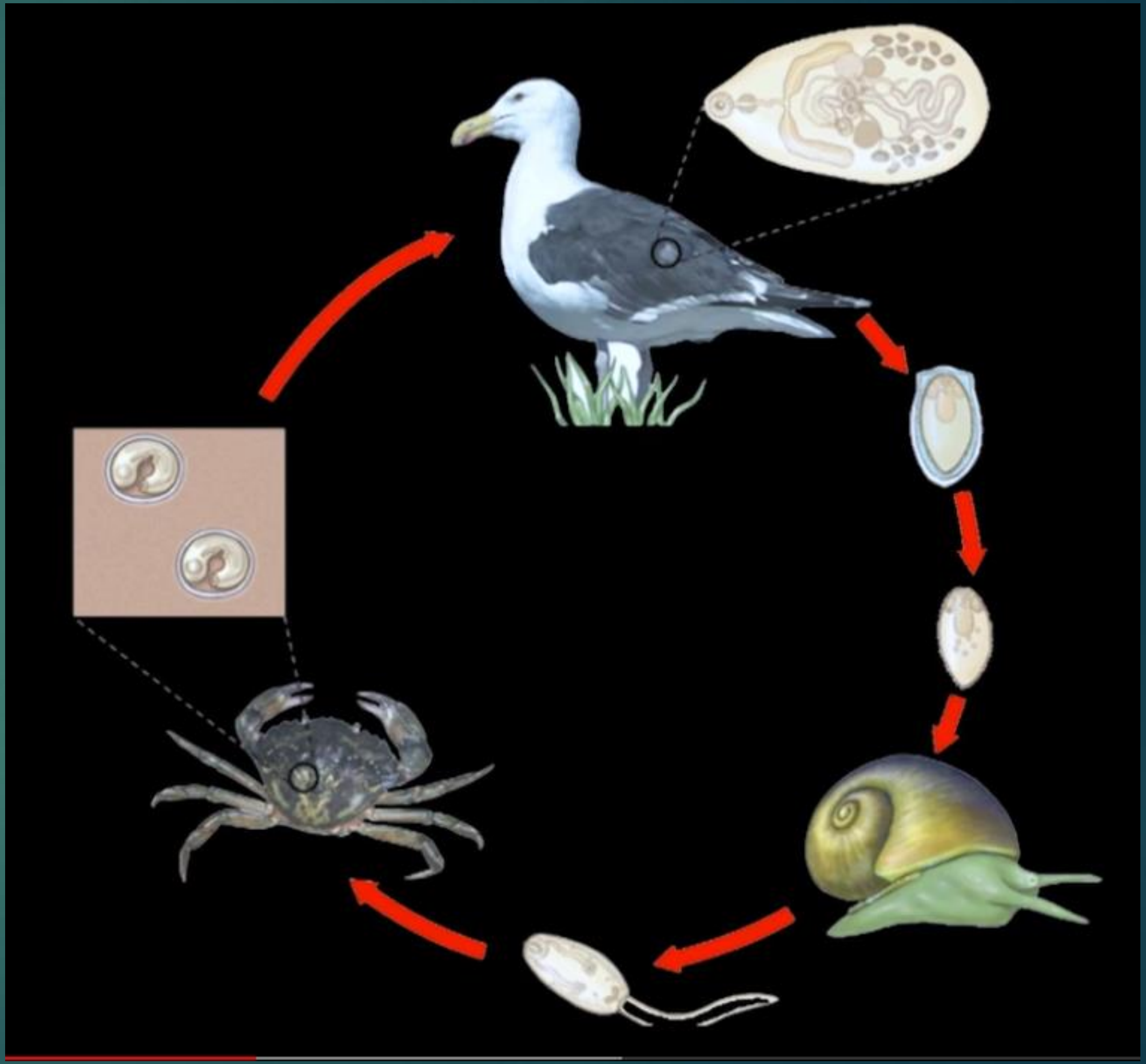
- About 40-50 percent of world's species are parasites
  - including viruses, bacteria, fungi, protozoans, insects, worms (lots), crustaceans, fish, plants ...
  - Parasites in turn have their own parasites: hyper-parasites

2 - High biomass: parasites are the elephant in the room

- Biomass = actual weight in an ecosystem
- Parasites = small, often microscopic, internal presence
- Study of salt marsh: weighted everything
  - Parasites were 3-9 x weight of bird biomass;
  - in one hectare area, equal to wgt of 2 elephants

3 - Integrative

- Parasites link and connect different species in an ecosystem
- They can fatigue their host & make them more vulnerable to predation
- Obligate multihost life cycles: parasite needs multiple free-living host species to complete its complex life cycle

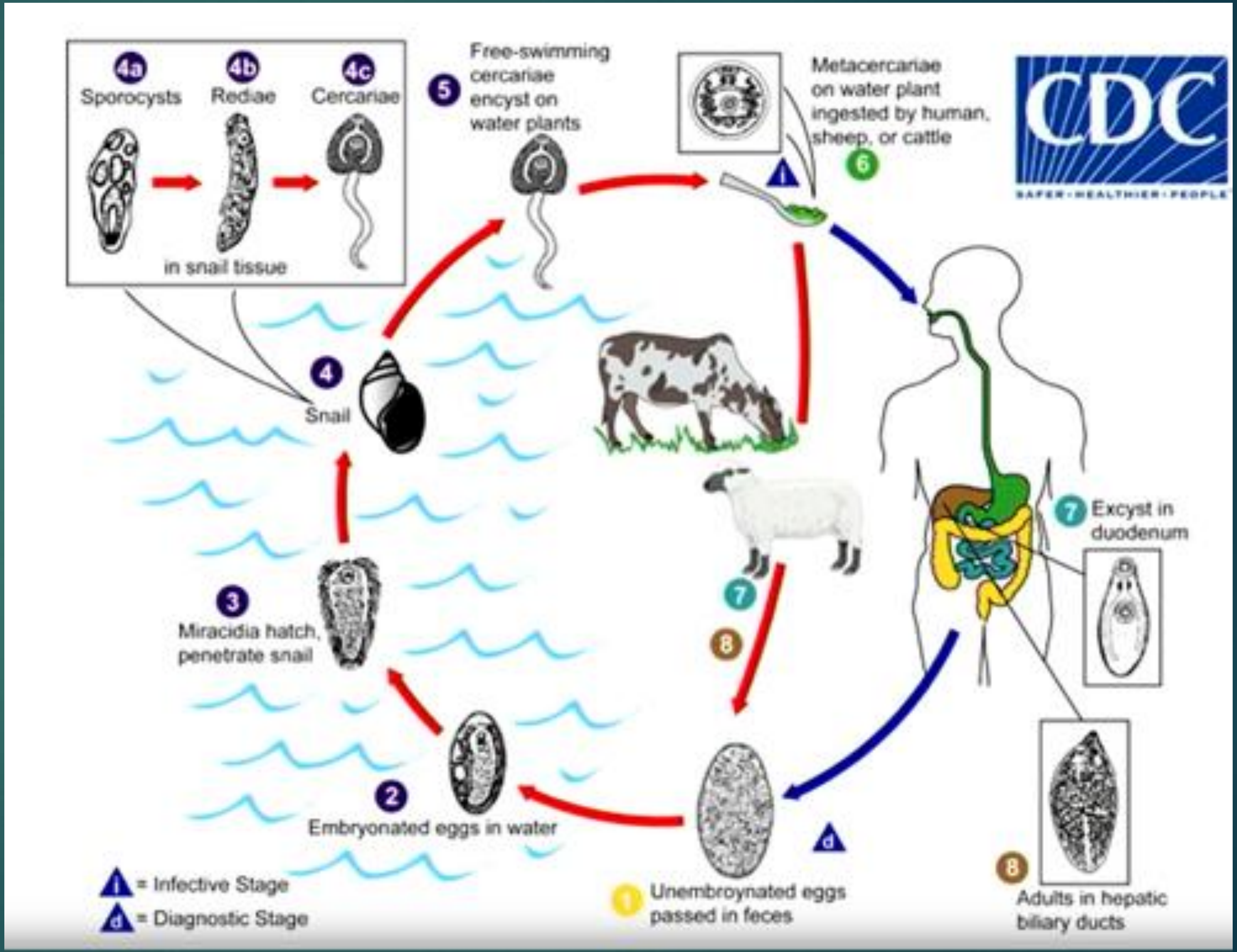


Complex life cycles, multiple hosts: Very hard to decipher

Snail-sheep-snail cycle for liver fluke, *Fasciola hepatica*

Worm first recognized in 1379 AD

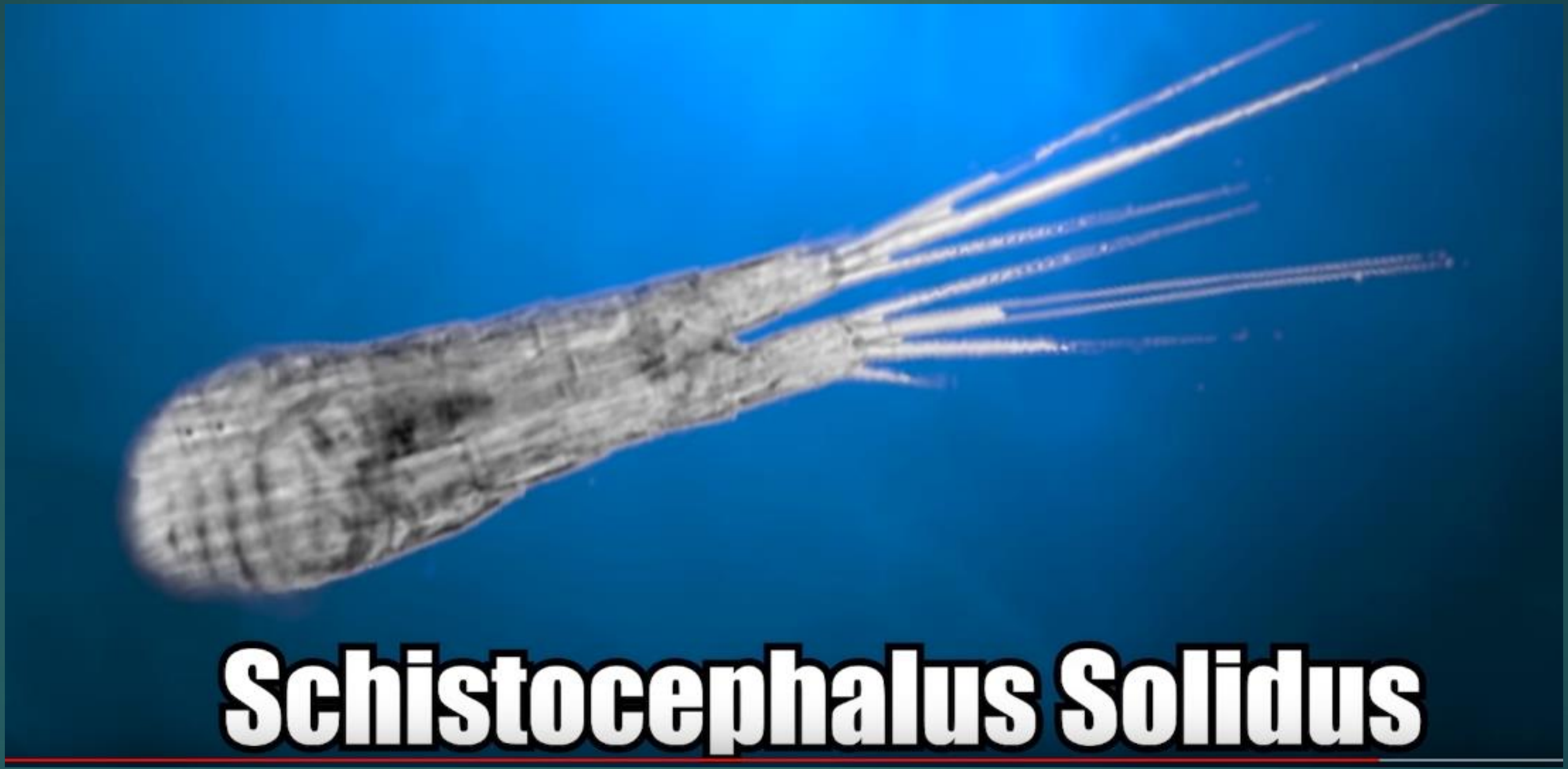
First trematode life cycle was worked out in 1881



Trematoda (flatworm, flukes) life cycle

- They are internal parasites of mollusks and vertebrates. Most trematodes have a complex life cycle with at least two hosts.
- Larval stage inside an intermediate host, in which asexual reproduction occurs, is usually a snail.
- Keeps it alive and makes it into a parasite larval production factory. Larva pumped into water where another host absorbs them; a crab, fish, worm, or another snail. Forms a cyst in it; until its final primary host eats it
- The primary host, where the flukes sexually reproduce, is a vertebrate. A shorebird. Becomes an adult producing eggs which are released in its feces.
- Feces eaten by snails which starts the cycle again
- Capability of evading immune systems of 3 hosts. Done without a brain or complex neural circuitry.

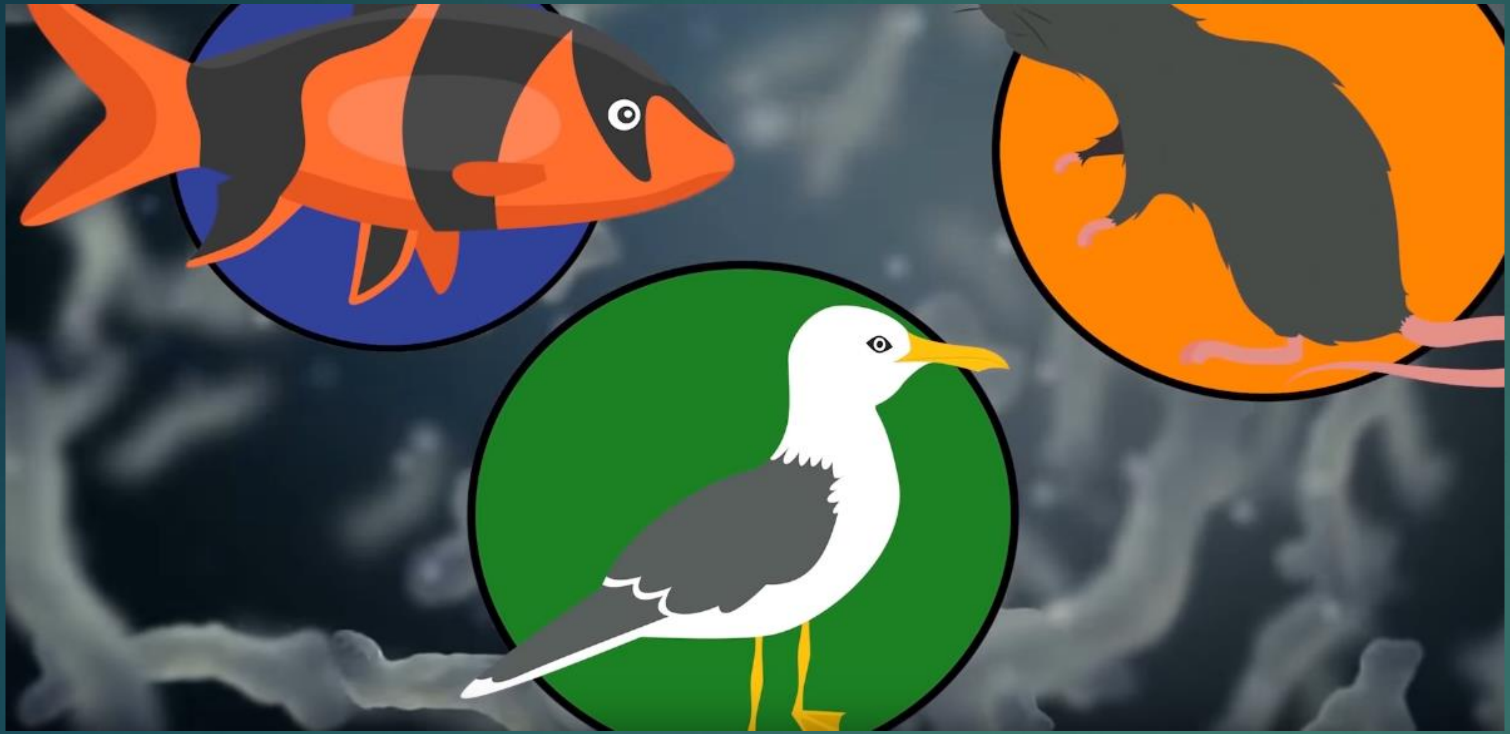
Fish tape worm



Schistocephalus solidus

- *Schistocephalus solidus* is a parasitic tapeworm with three different hosts, two intermediate and one definitive.
- In its adult stage the tapeworm resides in the intestine of fish-eating birds, where they reproduce and release eggs through the bird's feces.
- Free-swimming larvae hatch from the eggs, which are in turn ingested by crustaceans (the first intermediate host).
- The parasite grows and develops in the crustacean into a stage that can infect the second intermediate host, the three-spined stickleback (*Gasterosteus aculeatus*).
- The parasite's definitive host, a bird, then consumes the infected three-spined stickleback and the cycle is complete.

Fish tape worm 2



Develops inside bird intestine; feces into water were it becomes coracidium which infects a copedon crustacean; becomes hyperactive and eaten by a three-spined stickleback fish; bird eats fish

Importance of Parasites = Canaries in a coal mine: Parasites and healthy functioning ecosystems

- Parasites can indicate health or decline in ecosystem
- Marsh restoration project: shorebirds returned, restoring entire series of required life cycle species of parasites
- So number of parasites in snails are indicator of health of ecosystem
- 15 salt marshes in Maine study: number of parasites indicate number of free-living hosts, and physical and chemical aspects of marsh and human impacts (high road density)
- Parasites are canaries in coal mine (a bioindicator): when they decline, habitat is declining

Good parasite? Origin of parasitic lifestyle?

The sicker the better: nematode-infected passalus beetles provide enhanced ecosystem services: beetle is host to a naturally occurring nematode worm, *Chondronema passali*, which appears to cause little harm to the beetles. Parasitized beetles were 6% larger and eat 15% more wood. Some scientists think this originated parasitism in insects.

Evolution: Dawkins and Extended Phenotype

- Richard Dawkins, author of the landmark book *The Selfish Gene*.
- Genes evolve to make copies of themselves more successfully.
- Our bodies: nothing more than vehicles to get our genes intact into the next generation. = our genotype. Phenotype = all the bodily parts and functions that our genotype creates to advance its cause
- Dawkins realized that we don't have to limit phenotypes to the boundaries of our bodies. They also include the behaviors brought about by our genes.
- A beaver's genes encode its bones and muscles and fur. But they also encode the brain circuits that lead the beaver to gnaw at trees to build dams. The beaver benefits from the pond created by the dam in many ways. It's harder for predators to attack the beaver's lodge, because of deeper surrounding water. If a gene mutation gives rise to a beaver that builds even better dams; that particular beaver phenotype may stand a better chance of survival and, on average, have more baby beavers itself.
- From an evolutionary perspective, the dam—and even the pond that it creates—is as much an extension of the beaver's genes as its own body is.

Dawkins

- If the power of a gene can extend to manipulation of the physical world, Dawkins wondered, could it not extend as well to the manipulation of another living creature?
- Dawkins argued that it could, and he pointed to parasites as his prime example. The ability of a parasite to control the behavior of a host is encoded in its genes. If one of those genes mutated, the host's behavior would change.
- A mutation in a parasite that influences a host's behavior for the better will become more common. If a wasp acquires a mutation that compels its ladybug host to begin to act as a bodyguard, for example, its offspring carrying that trait will thrive, because fewer of them will be killed by predators.

Dawkins: Extended Phenotype

- Dawkins first developed these ideas in his 1982 book *The Extended Phenotype.* Proposed parasites as a model of the extended phenotype.
- If the power of a gene can extend to manipulation of the physical world, Dawkins wondered, could it not extend as well to the manipulation of another living creature?
- In the 1980s scientists had carefully studied only a few examples of parasites manipulating their hosts' behavior. But if the hypothesis was correct, there had to be genes within the parasites that trumped the genes in the hosts themselves that normally controlled their actions.
- Thirty-two years later, scientists are finally opening the black box of parasite mind control.

Host defenses vs parasitic wasps

- Parasitoid wasps face a range of obstacles by the host to egg laying, including behavioral, morphological, physiological and immunological defenses of their hosts.

- To thwart this, some wasps inundate their host with their eggs so as to overload its immune system's ability to encapsulate foreign bodies

- Others introduce a virus which interferes with the host's immune system.

- Some parasitoid wasps locate hosts by detecting the chemicals that plants release to defend against insect herbivores.

Evolution of multiple hosts

- For complex life cycles to emerge in parasites, the addition of intermediate host species must be beneficial, e.g., result in a higher fitness.
- It is probable that most parasites with complex life cycles evolved from simple life cycles.
- The transfer from simple to complex life cycles has been analyzed theoretically, and it has been shown that trophically transmitted parasites can be favored by the addition of an intermediate prey host if the population density of the intermediate host is higher than that of the definitive host. Also factors that catalyze this transfer are high predation rates, and a low natural mortality rate of the intermediate host.
- Parasites with a single host species are faced with the problem of not being able to survive in higher trophic levels and therefore dying with its prey host. The development of complex life cycles is most likely an adaptation of the parasite to survive in the predator.

Red Queen hypothesis

- Host–parasite coevolution: A general characteristic of many parasites is that they coevolved alongside their respective hosts.

- Correlated mutations between the two species enter them into an evolutionary arms race. Whichever organism, host or parasite, that cannot keep up with the other will be eliminated from their habitat, as the species with the higher average population fitness survives.

Red Queen hypothesis

- This race is known as the Red Queen hypothesis.
- The Red Queen hypothesis predicts that sexual reproduction allows a host to stay just ahead of its parasite, similar to the Red Queen's race in *Through the Looking-Glass*: "it takes all the running *you* can do, to keep in the same place".
- The host reproduces sexually, producing some offspring with immunity over its parasite, which then evolves in response.

Origin of Sexual reproduction

- The parasite–host relationship probably drove the prevalence of sexual reproduction over the more efficient asexual reproduction.
- It seems that when a parasite infects a host,
  - sexual reproduction affords a better chance of developing resistance (through variation in the next generation), giving sexual reproduction variability for fitness not seen in
  - the asexual reproduction, which produces another generation of the exactly the same organism susceptible to infection by the same parasite.
- Coevolution between host and parasite may accordingly be responsible for much of the genetic diversity seen in normal populations

Parasite-host co-evolution

- Coevolution of microbe parasite *Bacillus thuringiensis* and multicellular nematode host *Caenorhabditis elegans*
- Study: 48 host generations of experimental coevolution under controlled laboratory conditions
- Host–parasite coevolution caused multiple phenotypic and genetic changes in both interacting antagonists
- Two types of phenotypic responses were identified upon coevolution: reciprocal increases in virulence, resistance; and reciprocal reductions in growth rate and related traits, indicative of adaptation

Co-evolution: drives biological diversity

- Increases in genetic diversities under coevolution conditions: allele/gene frequency changes, within-population gene diversities, and across-population gene diversities

- Consistently elevated rates of genetic change, confirming the original formulation of the Red Queen hypothesis by Van Valen that persistence in a variable environment (such as that generated by interacting parasites and hosts) requires continuously high evolutionary rates.

- Charles Darwin hypothesized that parasites (among others) drive diversification and thus contribute to biological diversity

Parasitic plants

- 4000 known species of parasitic plants with representatives in 19 families of the plant kingdom.
- Sap suckers:
  - mistletoe,
  - dodder vine
  - strangler fig (kills host fig tree)
- Spanish moss is not a parasite; it is a neighbor

Dodder vine

Parasitism

Classic parasitoid wasp pattern

- Female wasp parasitizes small arthropods or arthropod egg by ovipositing their own egg into live host. Host attempts to encapsulate the egg. Parasite viruses counter this.
- The wasp eggs develop and hatch into larvae within the arthropod, and then the larvae consume the still-living host from the inside before emerging from its body to continue development.
- These wasps are known as parasitoids because infection is immediately lethal for the host, in contrast with conventional parasites that chronically feed on their hosts without causing sudden mortality.

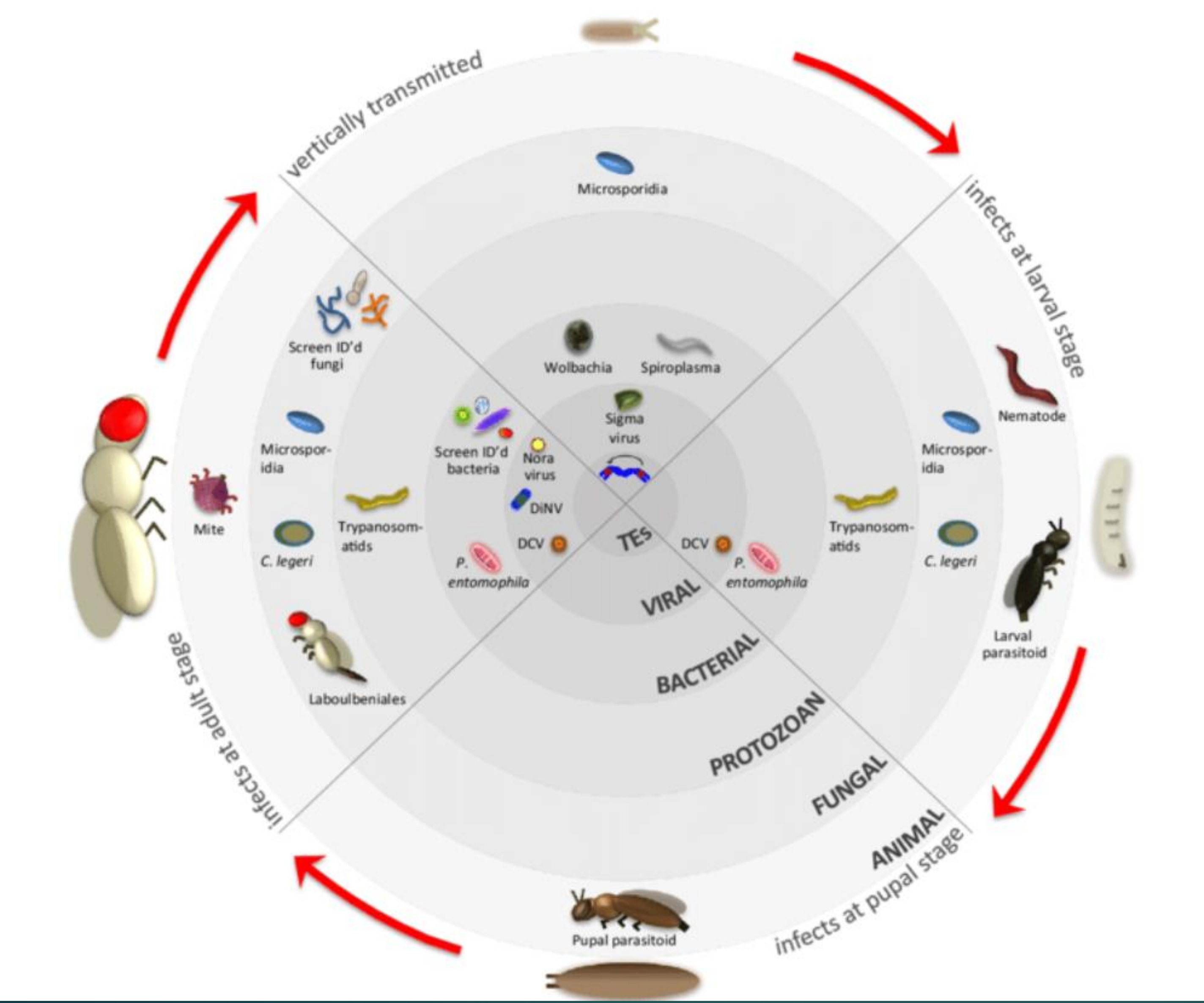
Daphnia magna is a small planktonic crustacean (adult length 2-5 mm)

- *D. magna* has become a model system to study the evolution and ecology of host-parasite interaction because of sheer number of its parasites

Daphnia magna

Taxa	*Parasite*	Tissue or infection site
Bacteria	*Pasteuria ramosa*	Blood, extracellular
	Spirobacillus cienkowskii	Blood, extracellular
Fungi	*Metschnikowia bicuspidata*	Body cavity, extracellular
Microsporidia	*Hamiltosporidium tvärminnensis*	Intracellular
	H. magnivora	Intracellular
	Glucoides intestinalis	Gut wall, intracellular
	Ordospora colligata	Gut wall, intracellular
Amoeba	*Pansporella perplexa*	Gut wall, extracellular
Chytrid fungus	*Caullerya mesnili*	Gut wall, intracellular
Nematoda	*Echinuria uncinata*	Body cavity, extracellular
Cestoda	*Cysticercus mirabilis*	Body cavity, extracellular

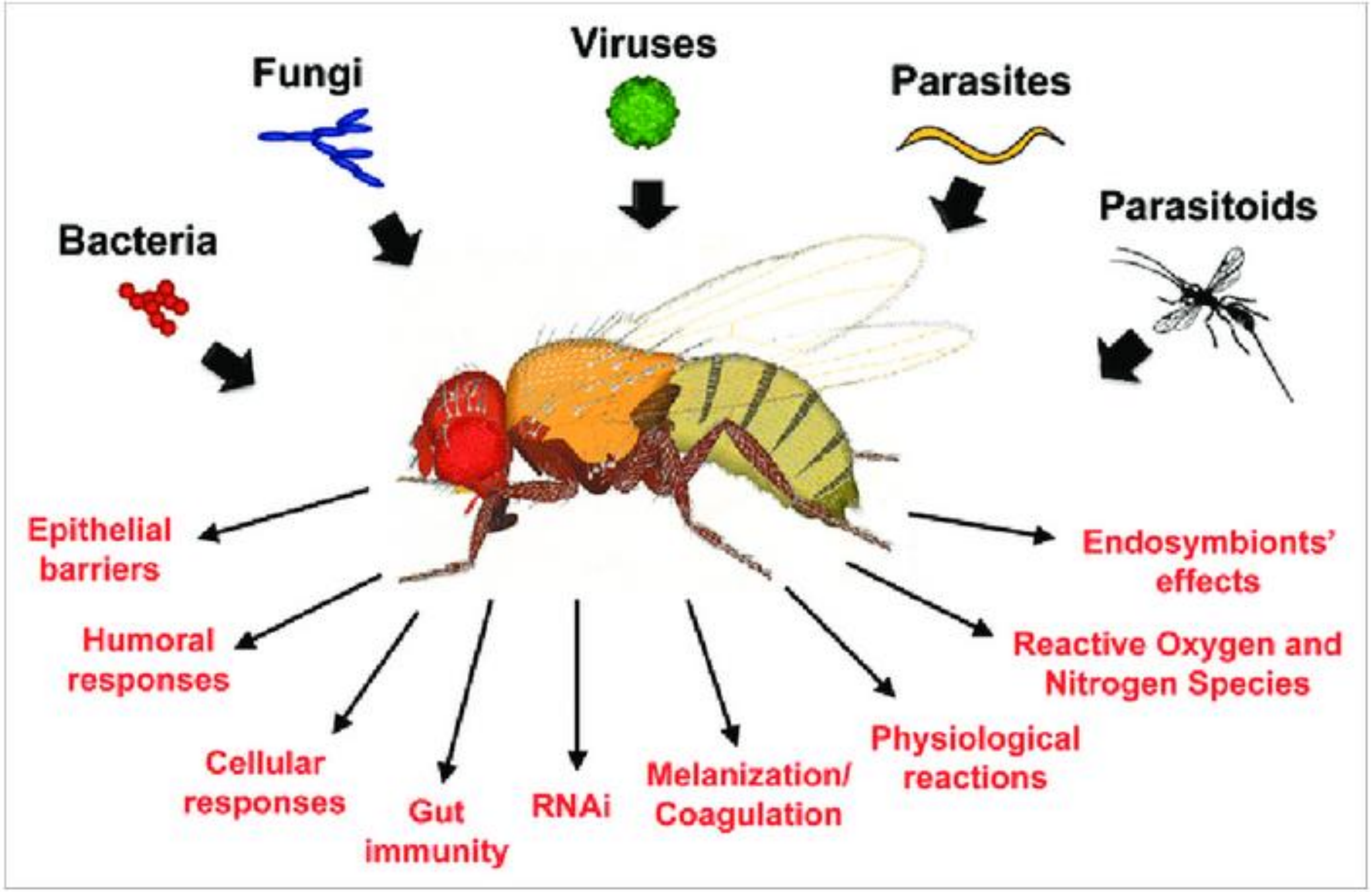
Parasites of Drosophila Melanogaster



Fruit Fly as model of Parasitism

Parasites effect it as a larva, pupa, & adult, as well as with vertical transmission during birth.
Only 20 of its parasites shown here.

Examples of Drosophila's enemies and defenses



Drosophila infection and immunity. Fruit flies can be experimentally challenged with bacteria, fungi, viruses, parasites and parasitoids, and respond to infection by activating a range of immune defense mechanisms (Fly cartoon was adapted from Flybase: http:// flybase.org/reports/FBim0000686.html).

A parasitic *Aleiodes indiscretus* mummy wasp deposits her eggs on a gypsy moth caterpillar.
She deposits eggs in the caterpillars.
The eggs hatch and the wasp larva feeds on the caterpillar, leaving a hardened caterpillar skin, or mummy.
The wasp pupates within the mummy and eventually the adult breaks out, leaving a small hole in the husk of the caterpillar.

Parasitoid Wasps: Ichneumonidae

- The parasitoid wasps include some 25,000 Ichneumonoidea, 22,000 Chalcidoidea, 17,000 Braconidae, 5,500 Vespoidea, 4,000 Platygastroidea, 3,000 Chrysidoidea, 2,300 Cynipoidea, and many smaller families

- **Ichneumonidae:** Parasitoid wasp family within the insect order Hymenoptera (bees, ants).

- Only 25,000 species described (of estimated 100 K); The family has existed since at least the Early Cretaceous (c. 125 Ma)

- It is one of the major regulators of invertebrate populations. It is quite common for 10-20% or more of a host's population to be parasitized/

Parasitoid Wasps: Ichneumonidae

- Have an ovipositor which they use to lay eggs inside or on their host

- Hosts: butterflies, moths, beetles, wasps, bees, flies, ants

- Parasitoids are among the most widely used biological control agents. Classic biological pest control using natural enemies of pests (parasitoids or predators) is extremely cost effective. i.e. *Encarsia formosa*, a wasp, bred commercially to control whitefly in greenhouses

Two types of wasps: where the egg is deposited

- They can be divided by where they lay their eggs.
  - Endoparasitic wasps insert their eggs inside their host, allowing the host to continue to grow (thus providing more food to the wasp larvae), molt, and evade predators.
  - Ectoparasitic wasps deposit eggs outside the host's body, immediately paralyzing the host to prevent it from escaping or throwing off the parasite. They often carry the host to a nest where it will remain undisturbed for the wasp larva to feed on.
  - Most species of wasps do not attack adults, but rather the eggs or larvae of their host,

Parasitic flatworm Ribeiroia ondatrae & American Bullfrog Lithobates catesbeianus

- After the flatworm Ribeiroia ondatrae reproduces asexually inside a snail, its larvae find a bullfrog tadpole and burrow their way through its skin, forming cysts around the frog’s developing limbs.
- Produces limb malformations, particularly missing, malformed, and additional hind legs. The ungainly victim is easy prey for frogeating birds like herons.
- Inside the heron, the parasite reproduces sexually.
- Its eggs reenter the water when the bird defecates, infecting new snails.

Parasite that replaces a fish's tongue

Potter wasp: Food, but poor mothering

Potter wasp, building a mud nest; she will provision it with paralyzed insects, on which she will lay her eggs; she will then seal the nest and provide no further care for her young

Beewolf wasp (*Philanthus triangulum*) and honeybees

Stings and buries honeybee and lays one egg on it

The tunnel of *Philanthus triangulum* can be as much as 1 m long. Up to 34 lateral tunnels, each ending in a brood chamber, branch off from the main tunnel. Each brood chamber is stocked with one to six honeybees.[

A. borealis fly ovipositing eggs into the abdomen of a worker honeybee

- These flies are colloquially known as **zombie flies** and the bees they infect are colloquially known as **zombees**

- Parasitized bees appear to be drawn to light sources at night.

- Hive abandonment, particularly at night, has been implicated as a behavior modification of *A. borealis*

Parasitic fly: Apocephalus borealis

- Causes bee to abandon their nest, flying from it at night and soon dying, allowing the next generation of flies to emerge outside the hive
- Paper wasps, honey bees, bumble bees: part of colony collapse disorder

Female phorid fly *Apocephalus borealis* (centre left) ovipositing into the

Fire ant parasitic flies (*Pseudacteon tricuspis*): Ant decapitation

- In fire ant parasitic flies (*Pseudacteon tricuspis*), the female will strike an ant and inject an egg into the ant's (*Solenopsis invicta*) body.
- After the larva hatches, it moves into the ant's head and feeds mostly on hemolymph (the equivalent of blood in insect) until just prior to pupation.
- Ant leaves colony & moves up to 50 meters away from the nest and towards a moist, leafy place where they can hatch safely
- Eventually the larva completely devours the ant's brain, which often falls off (hence the species nickname: "decapitating fly"). The larva then pupates in the empty head capsule, emerging as an adult fly after two weeks.

(Henne and Johnson, 2007

20 species of Pseudacteon: tiny Ant decapitating Phorid fly

Fly develops and pops out of ant’s head

Then releases a chemical that pops the ant’s head off. Safely inside the brain, the fly pupates in the detached head capsule, requiring a further two weeks before emerging through the ant's mouth.

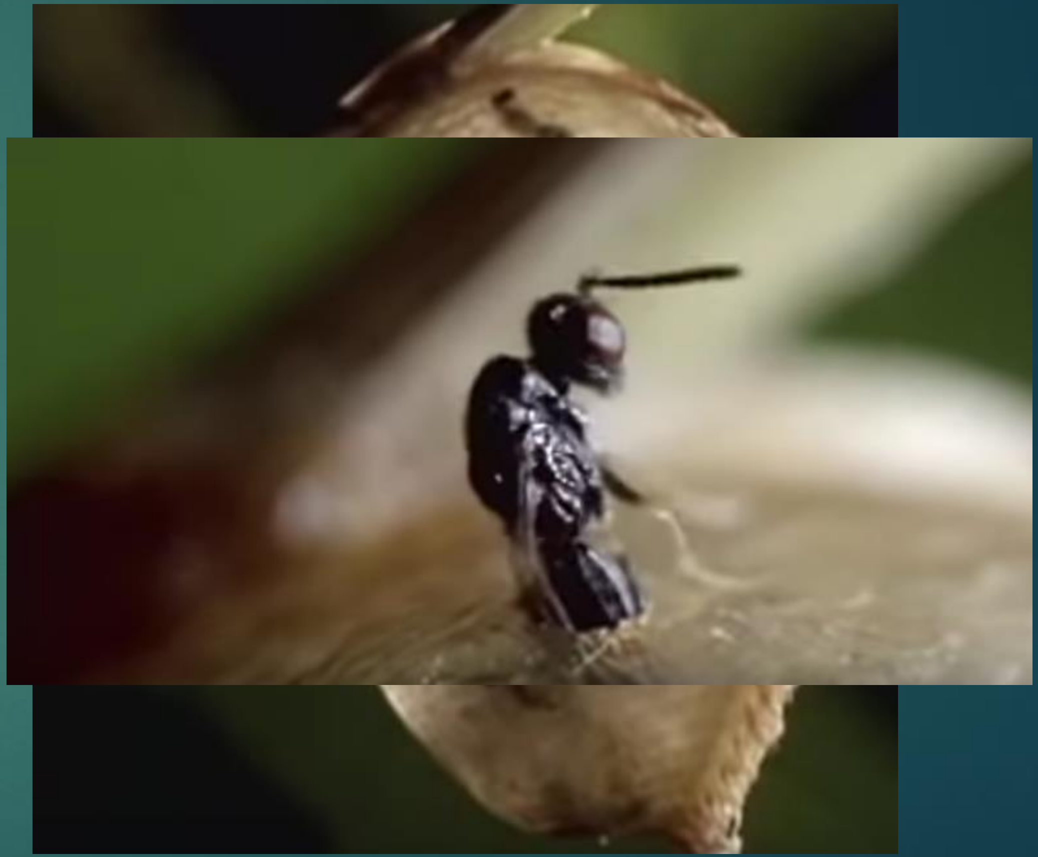
Host: fire-ants of South America

US now imports these flies to combat invasive fire ants

Preying Mantis: protects egg in tough skinned bubble

But Wasp still penetrates it

Both *P. Mantis* and new wasps survive



Brood Parasite: caterpillar (*Phengaris rebeli*): Mountain Alcon blue butterfly

- Caterpillar (*Phengaris rebeli*) mimics ant (*Myrmica schencki*) surface chemistry and the sounds they use to communicate, allowing it to penetrate the ant colony undetected and lays larva that are cared for by the ants.
- They are in turn the victims of a parasitoid wasp (*Ichneumon eumerus*) which deposits its eggs into the eggs of P. rebeli. The hyperwasp's offsprings emerge later as adults from the caterpillar cocoon.
- The wasp seeks the caterpillar host by first detecting the ant colonies. The body surface chemicals expressed by the wasp induce aggression in ants, leading to in-fighting between the ants. This distraction permits the wasp to penetrate the nest and attack the caterpillar host.

Alcon Blue Butterfly (*Phengaris rebeli*): A Devious, Deceitful Cycle of Life: Brood Parasite

Brood parasites: Few adapatations are more convenient than tricking other creatures into caring for your young, like classic cuckoo bird, which lays its eggs in other birds' nests.

Alcon caterpillars secrete chemicals similar to those used by local ants to communicate. Ants adopt Alcons after finding them newly hatched from eggs laid on leaves, then nurture them for up to two years while their own young go untended

Ants mothering Butterfly larva

Ichneumon eumerus wasp: creates ant civil war

- Alcon blue butterfly has a nemesis, the *Ichneumon eumerus* wasp. It seeks the underground *P. alcon* caterpillar.
- When the wasp detects an Alcon caterpillar inside an ant colony, it charges inside and sprays a pheromone cocktail that makes the ants attack each other.
- The wasp slips through the confusion, lays its eggs inside the chrysalis and leaves.
- The hyper parasite eggs hatch and consume it from the inside.

Sacculina carcini – parasitic barnacle

Male crabs are feminized so they can carry more of parasite

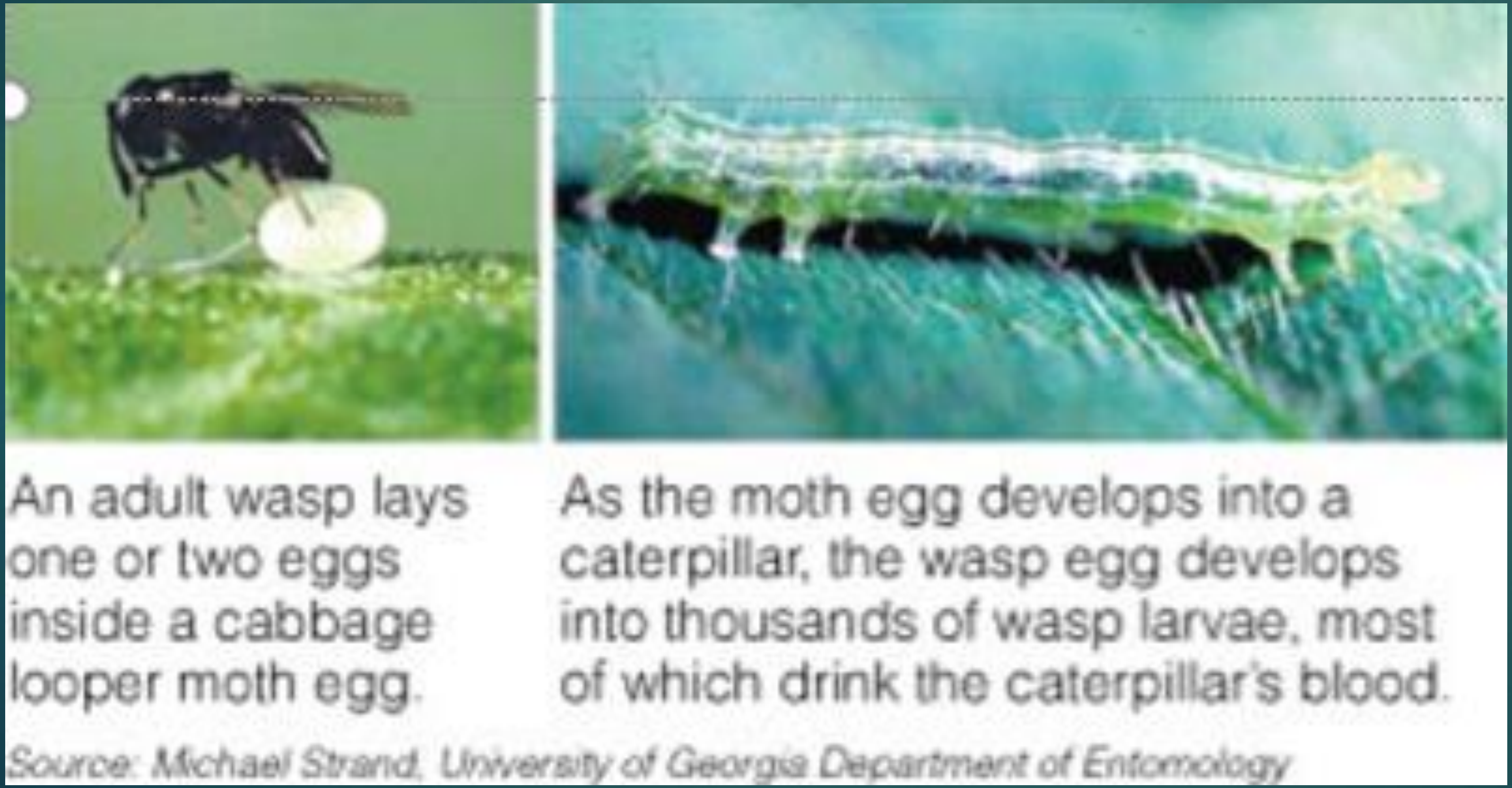
Rhizocephala: another parasitic barnacle that infects sheep crab which it feminizes to use as its egg sack

White spots are baby barnacles ready to go infect

Sci-fi life cycle of the wasp Copidosoma flondanum

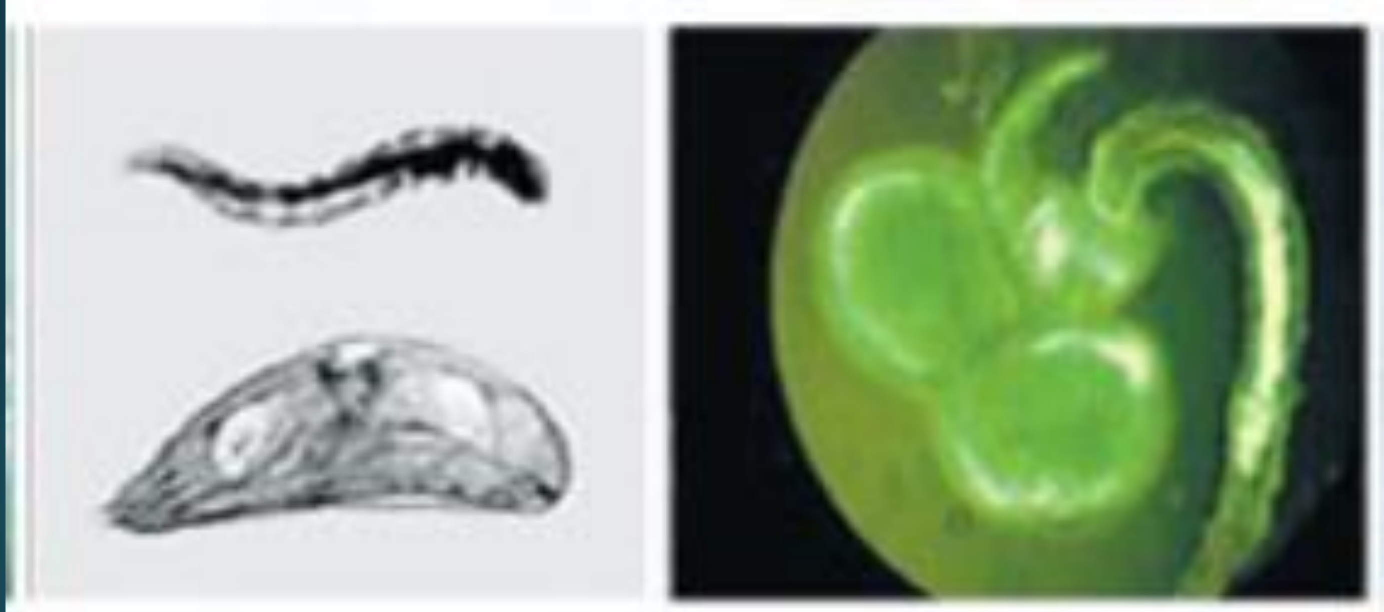
Homicidal, Fratricidal, Suicidal Larvae: The strange life cycle of Copudosoma fkxidanum. A wasp that produces largest recorded brood

.



Wasp lays 1 male and 1 female egg. Each grapelike mass of cells develops into a wasp embryo. A single egg can give rise to more than 3,000 genetically identical siblings, each about a fifth of an inch long.
"The caterpillar is about two to three inches long, so you can stuff a lot of wasps in there,"

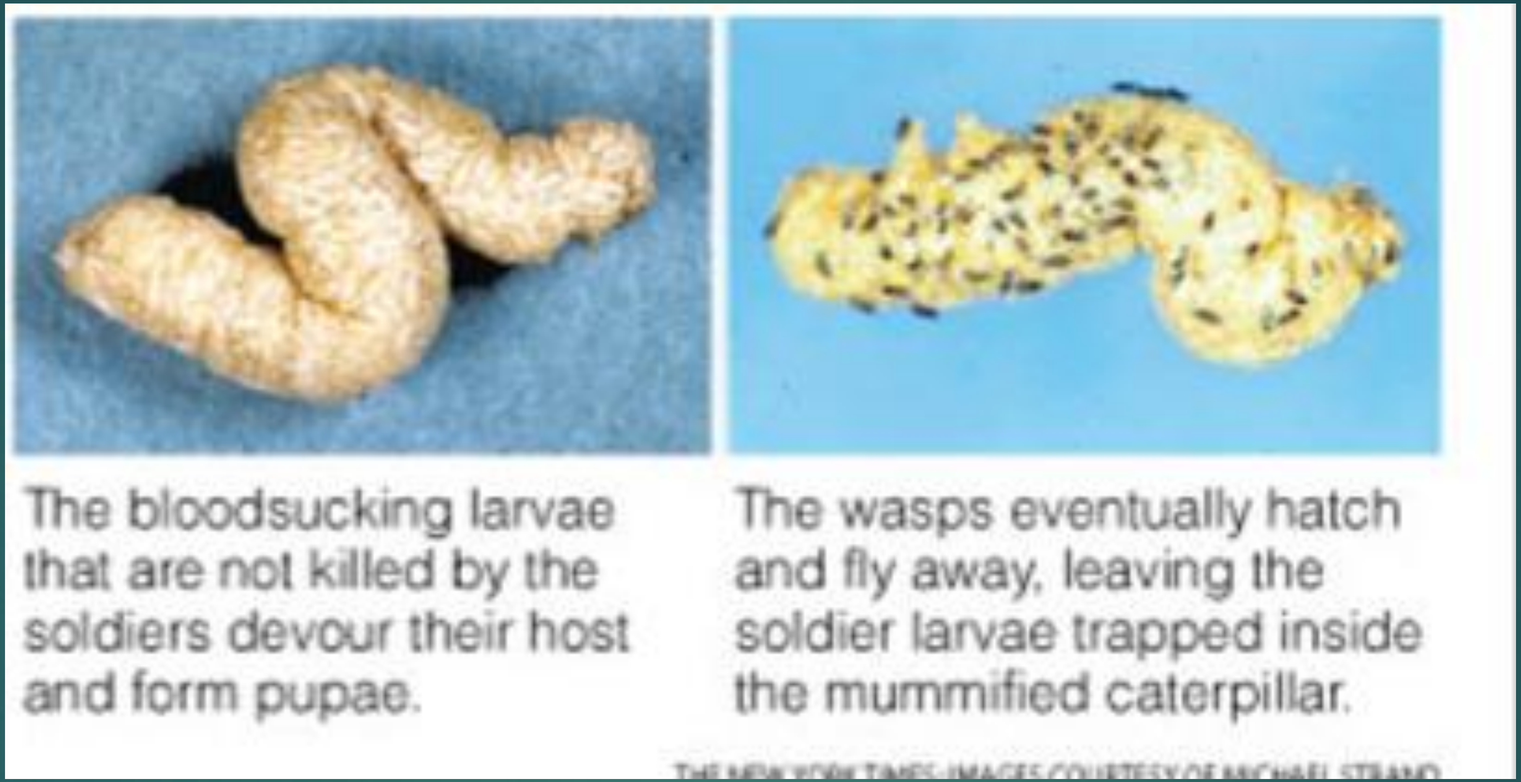
Homicidal siblings



Up to a quarter of the larvae take on snakelike "soldier" forms (top left) that attack larvae from other wasps or from rival eggs of the same mother.

- Most of the larvae are maggotlike creatures that drink the caterpillar's blood.
- Up to a quarter of the wasps, mostly females, become soldiers with an entirely different form. They develop slender, snakelike bodies and rasping jaws.
- These hundreds of soldiers attack other wasp larvae. By killing off competitors, they increase the odds that their genetically identical siblings will survive and have

Fratricidal



The blood-suckers that are not killed by the soldiers eventually begin to devour the organs of their host, become pupae, and then develop into female adults that fly away, leaving their male soldier brothers to die. One case of 2000 female surviviors, and 1 male brother left.

Tale of the Hawaiian Crickets

- An example of fast evolution:
- Over 10 years male field crickets (*Teleogryllus oceanicus*) on the Hawaiian island of Kauai fell silent.
- By 2001, only a single male cricket was heard and crickets were hard to find.
- In 2003 the crickets were back but their song was silent.
- The original cause of the silence had been the arrival on the island of a deadly parasitoid fly (*Ormia ochracea*) which uses a male cricket's song to find him, parasitizing with her maggots which then eat him alive.
- World's best hearing aide microphone based on hearing design of this fly.

Silent crickets

- Only silent male crickets survived the fly.
- Surviving male crickets had previously rare form of wing which lacked "scraper" used to make sound.
- Under selection pressure from the fly, mutant silent males went from rare to common in 20 generations.
- Also a different island cricket developed different gene with same wing effect. Independent convergent evolution.

Aphids and their Parasitic Wasp (Aphidius ervi)

Wasp Burial ritual film

Behavior Modification
by Parasites

Neuro-Parasitology

- Parasitism = All about getting into the next host for survival
- Some parasites have evolved to “hijack” the central nervous systems of a host to manipulate its behavior.
- Parasites can manipulate behavior of a host. These behavior modifying parasites have been called:
  - ‘puppet-masters’
  - ‘evolutionary neuroscientists’
  - ‘evolution’s neurobiologists’
  - ‘neuroparasitology’

Neuro-parasitology

- Neuro-parasitology is an emerging branch of science that deals with parasites that can control the nervous system of the host. It offers the possibility of discovering how one species (the parasite) modifies a particular neural network, and thus particular behaviors, of another species (the host).

- Insects are not just automatons. They are capable of non-random endogenous process of behavioral choice, which might imply a precursor motif of “spontaneous” behavior (as opposed to reflexive behavior).

- In some of the most fascinating manipulations, the parasite taps into the host brain neuronal circuities to manipulate hosts brain functions.

Frederic Libersat, et al., 2018

Neuro-parasitology

- Certain parasites have been shown to affect
  - (1) navigation of the host that leads to a suicidal behavior;
  - (2) induce bodyguard behavior;
  - (3) affect the host’s motivation to move;
  - (4) when infected, show “antisocial” behavior.
  - (5) when infected, show atypical behaviors for that species

- To exert long-term behavioral manipulation of the host, parasite must secrete compounds that act through secondary messengers and/or directly on genes often modifying gene expression to produce long-lasting effects.

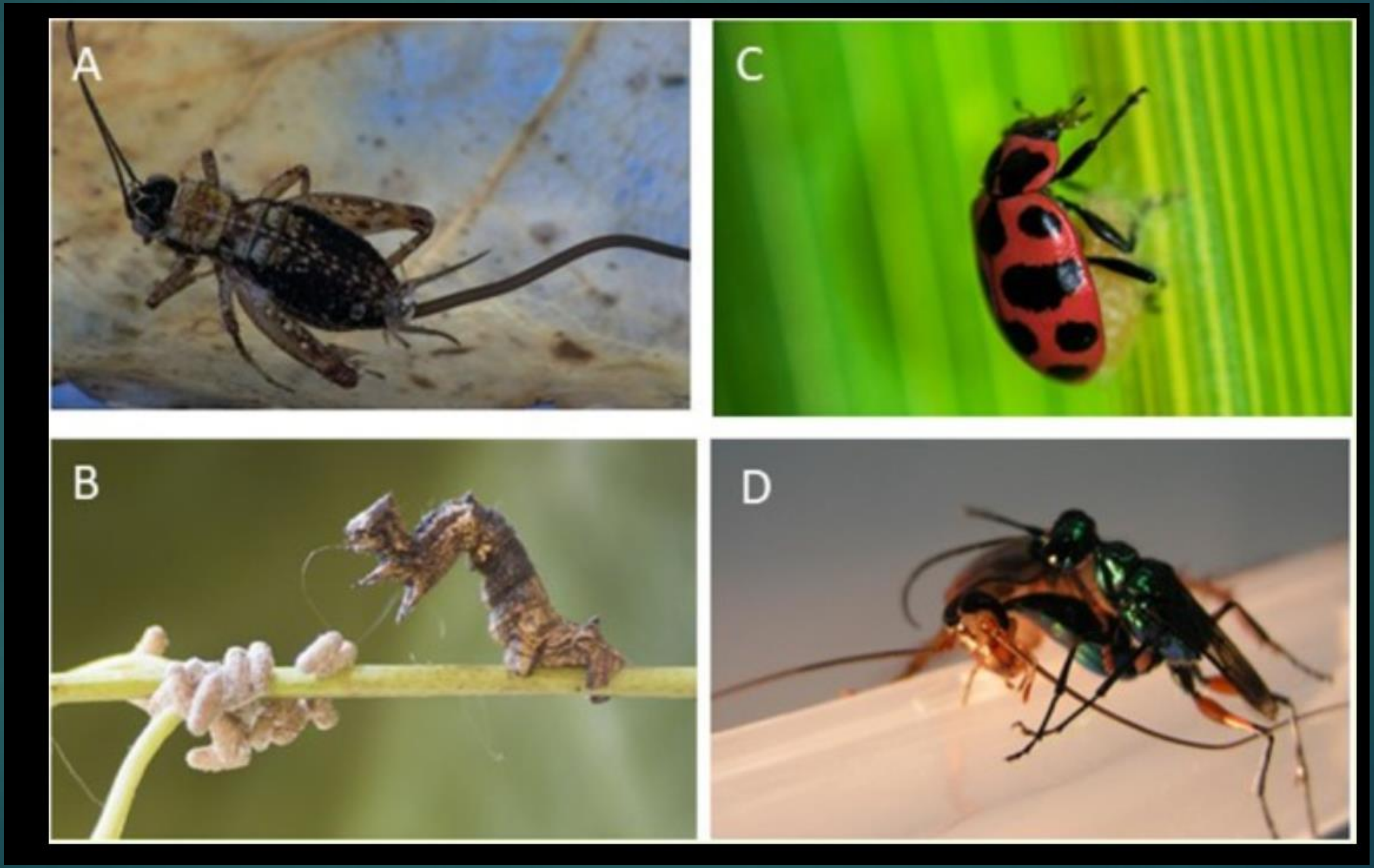
Extreme form of this parasitic life cycle involves host behavioral modification

- Some parasites are capable of modifying the behavior of its host in order to get into next host.
- Examples:
- Broodsac snail: make snail eye socket look like pulsating caterpillar; birds prefer infected vs uninfected snails
- A parasitic worm turns a tropical ant berry-red and causes it to climb high, attractive prey for birds, the worm’s next host.
- A mouse infected by toxoplasma gondii no longer fears cats.
- A jewel wasp precisely injects neurotoxins into its cockroach prey’s brain.

Zombies

- Zombies really exist in nature.
- Usually "zombies" in nature are the result of a parasitic relationship. This type of relationship is when one member of the pairing benefits while the other is harmed.
- There are an array of parasites that include plants, viruses, fungi, protozoa, wasps, and tapeworms.
- Parasites have different goals when invading a host.
  - Some simply use the host's resources with no intention of killing them as they need the host to survive.
  - Others hijack the nervous systems of their hosts and make them "zombies" by altering their behavior, which many times results in the host's demise.

Brain control in insects



Tapeworm castrates shrimp, turns them from transparent to red in color, makes them live longer, and become sociable and swim in groups.

It’s complicated life cycle, ends in the greater flamingo where it reproduces.

Fatal Attraction

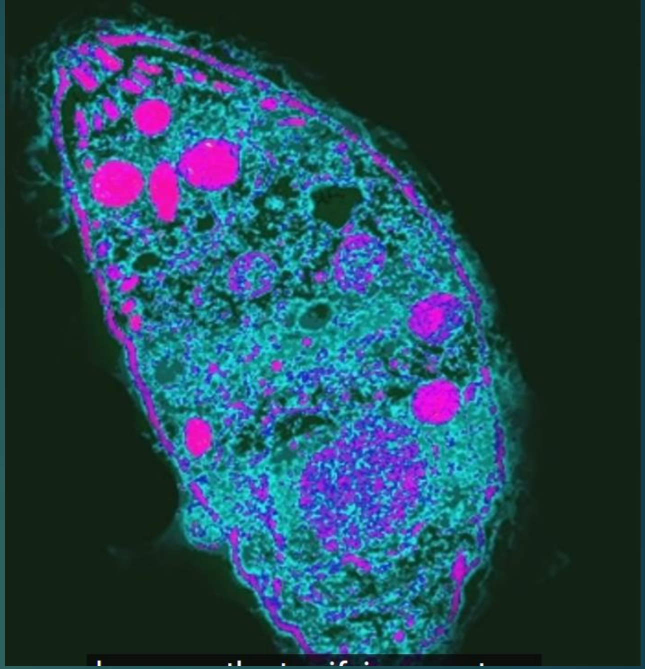
Some infected mice and rats show ‘fatal attraction’

Kochanowsky & Koshy (2018) Toxoplasma gondii. *Current Biology* 28: R770-R771.

But no field studies of wild mice being eaten more often

Toxoplasma gondii

- Infiltrates rats, cats, sometimes humans (present 30% of humans via undercooked pork or lamb)
- Can only reproduce in a cat
- Present in cat feces. Rat/mouse gets infected. Toxo releases dopamine.
- Rat switches from avoidance to attraction to smell of feline urine
- Cat eats rat/mouse. Toxo gets to have sex.
- Classic tale of Eat, Prey, Love.



Toxoplasma lifecycle

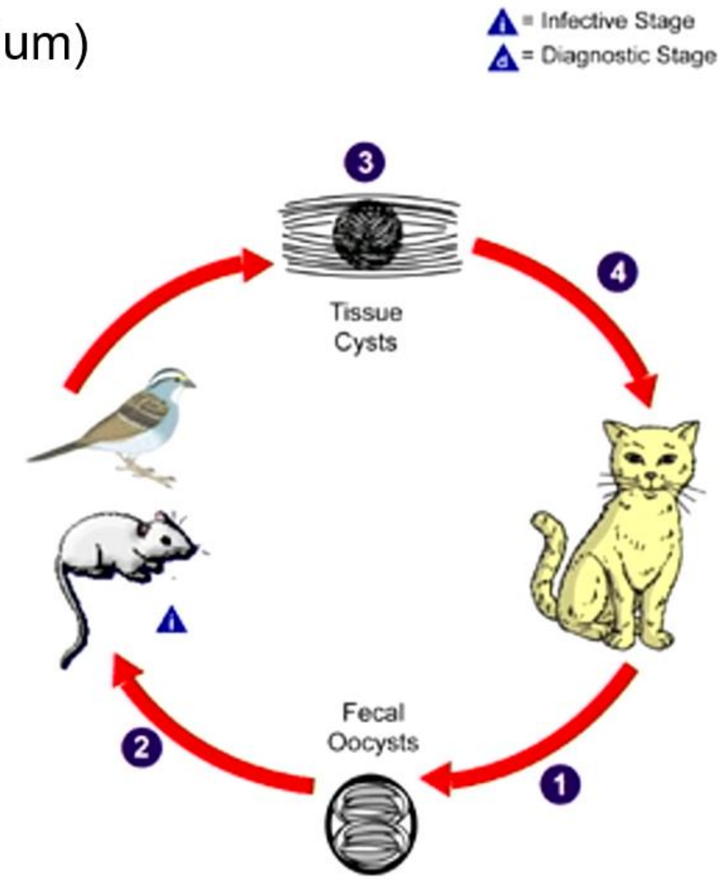
Obligate intracellar protozoan parasite
(same family as malaria and Cryptoporidium)

Sexually reproduces in cat's gut

Removes fear response to cat odour
(but other predator odours still give fear)

Sexually transmitted in rats, makes
male rats more attractive to females

Cysts in brain – especially in nerves

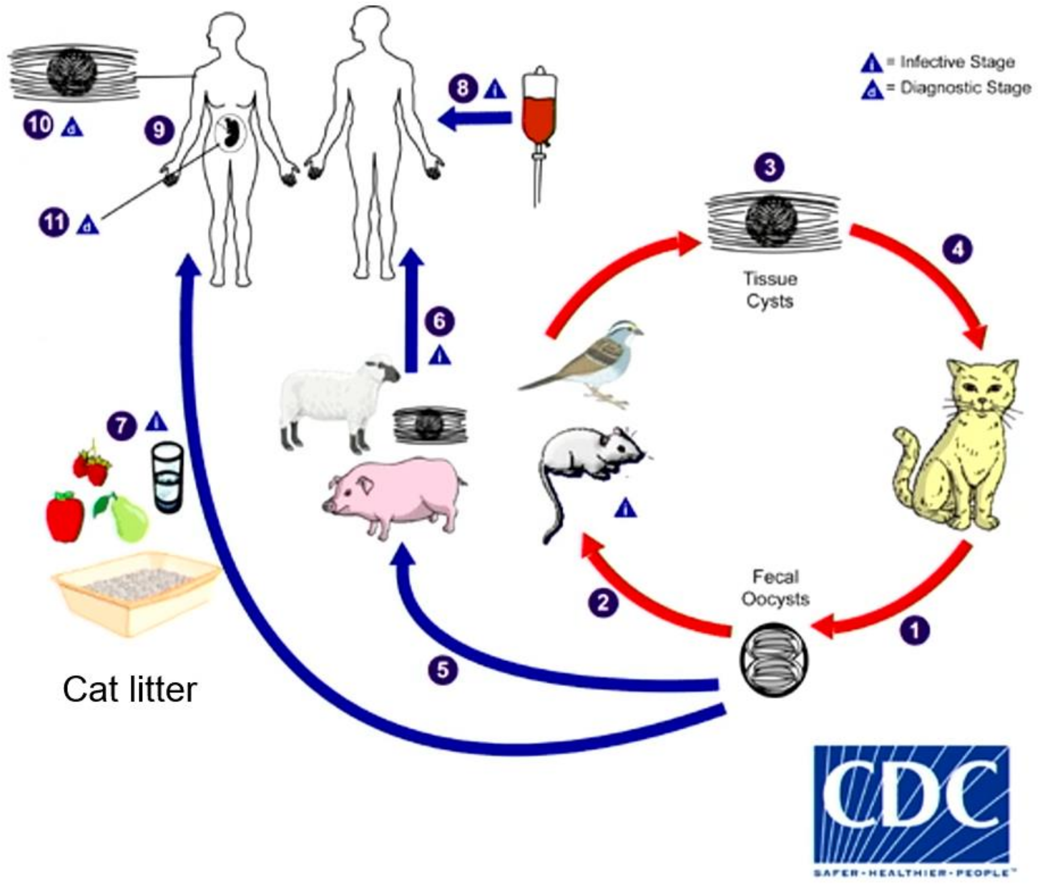


Vyas, A (2015) Mechanisms of host behavioral change in *Toxoplasma gondii* rodent association. *PLoS Pathog* 11:
Kochanowsky & Koshy (2018) Toxoplasma gondii. *Current Biology* 28: R770-R771.

www.cdc.gov/parasites/toxoplasmosis/biology.html

Toxoplasma lifecycle in humans

Human latent infection
~15 - 90% depending on country & population



www.cdc.gov/parasites/toxoplasmosis/biology.html

50-90% of humans have latent or benign presence of Toxo. Only if immune compromised, i.e. AIDS. Also fetuses in pregnant women, transfusions, food

Does *Toxo* affect human behavior?

- Examples:
- Flegr, et al (2009) Increased incidence of traffic accidents in *Toxoplasma- infected* military drivers and protective effect RhD molecule revealed by a large- scale prospective cohort study. *BMC Infect Dis* 9: 72.
  - 2.5 x higher accident rate
- Flegr, J (2013) How and why *Toxoplasma* makes us crazy. *Trends in Parasitology* 29: 156-163.
  - Some cases of schizophrenia
- Johnson et al (2018) Risky business: linking *T gondii* infection and entrepreneurship behaviours across individuals and countries. Proc RS B 285.
  - 2.5 x more likely you start a business

  - Correlational studies

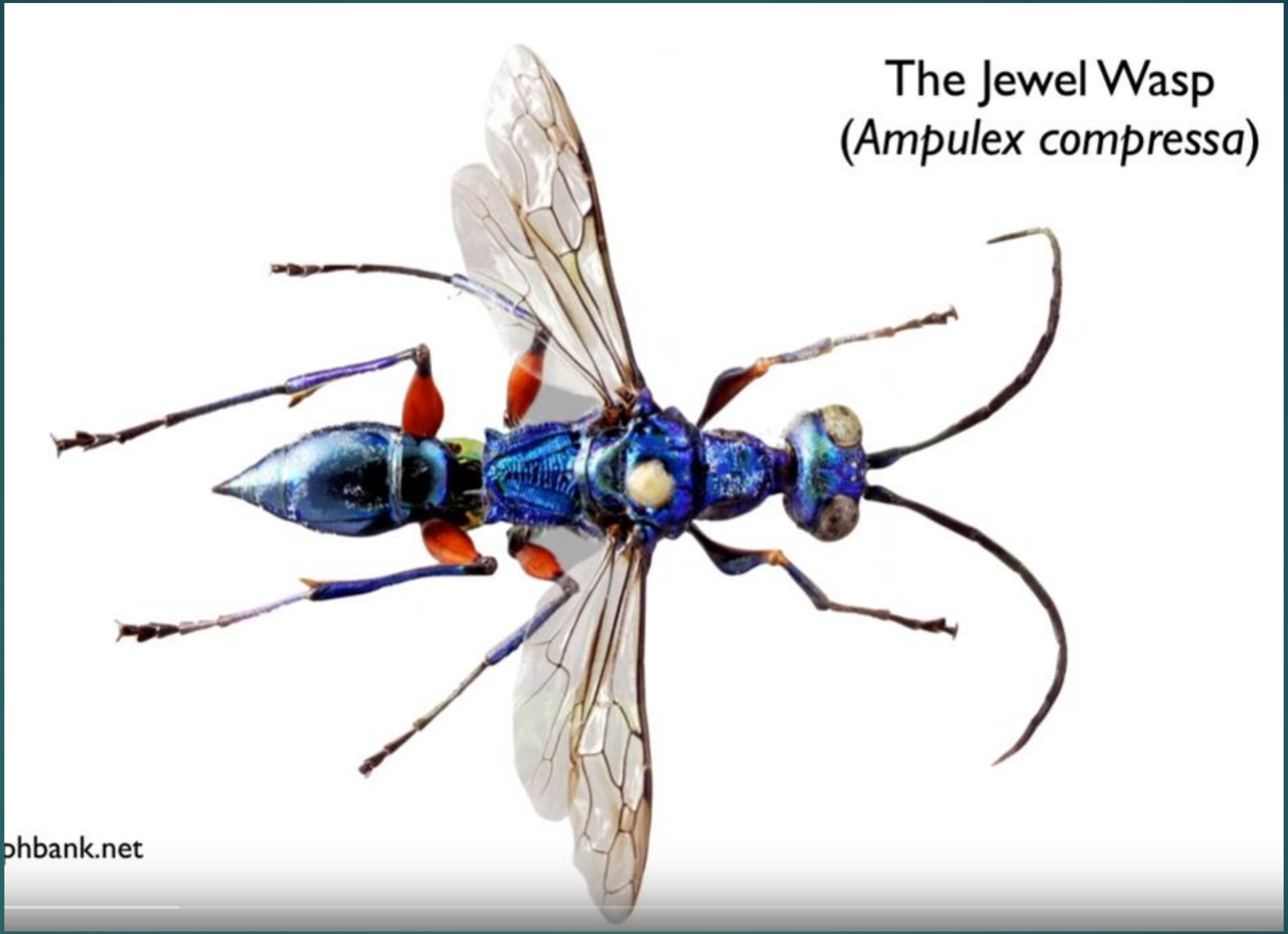
- People suffering from road rage or other impulsive anger disorders are twice as likely to have been exposed

But does *Toxo really* adaptively manipulate rodent hosts?

- Worth et al (2013) Adaptive host manipulation by *Toxoplasma gondii*: fact or fiction? *Trends in Parasitology* 29: 150-155.
  - Inconsistencies in experimental results (rat anxiety vs urine effect, etc.)
  - no evidence that it does increase predation in the wild
  - no evidence that sexual stage is essential

Toxo, chimps and leopards

- 2016 study tested chimpanzees, which are still preyed upon in their natural environment by leopards.
- The behavioral test centered on olfactory cues showed that, whereas uninfected individuals avoided leopard urine, parasitized individuals lost this aversion.
- Hence, when big cats were chasing our ancestors, *T. gondii* manipulative skills could have evolved because early hominids were suitable intermediate hosts.



The emerald jewel wasp (Ampulex compressa) is renowned for its ability to zombify the American cockroach (Periplaneta americana) with a sting to its brain.
The wasp then takes the cockroach for a walk.

Queen of all parasitic wasps

Jewel wasp and American cockroach

Photo: Fred Libersat

Cockroach

Periplaneta americana:

It’s host

Co-evolution

- One such example is the parasitoid Jewel Wasp (Ampulex compressa) which specifically depresses the drive of its prey to engage in locomotion

- The parasitoid Jewel Wasp hunts cockroaches to serve as a live food supply for its offspring. The wasp stings the cockroach in the head and delivers a cocktail of neurotoxins directly inside the prey's cerebral ganglia. Although not paralyzed, the stung cockroach becomes a living yet docile ‘zombie’, incapable of self-initiating spontaneous or evoked walking.

Opponents

Cockroaches fight back

Movie S1

Kicking Defense Filmed at
1000 frames/second

Catania, KC (2018) How not to be turned into a zombie. *Brain Behavior and Evolution* 92: 32-46.

Each frame is 1000th of a second; Roach wins 50% of time

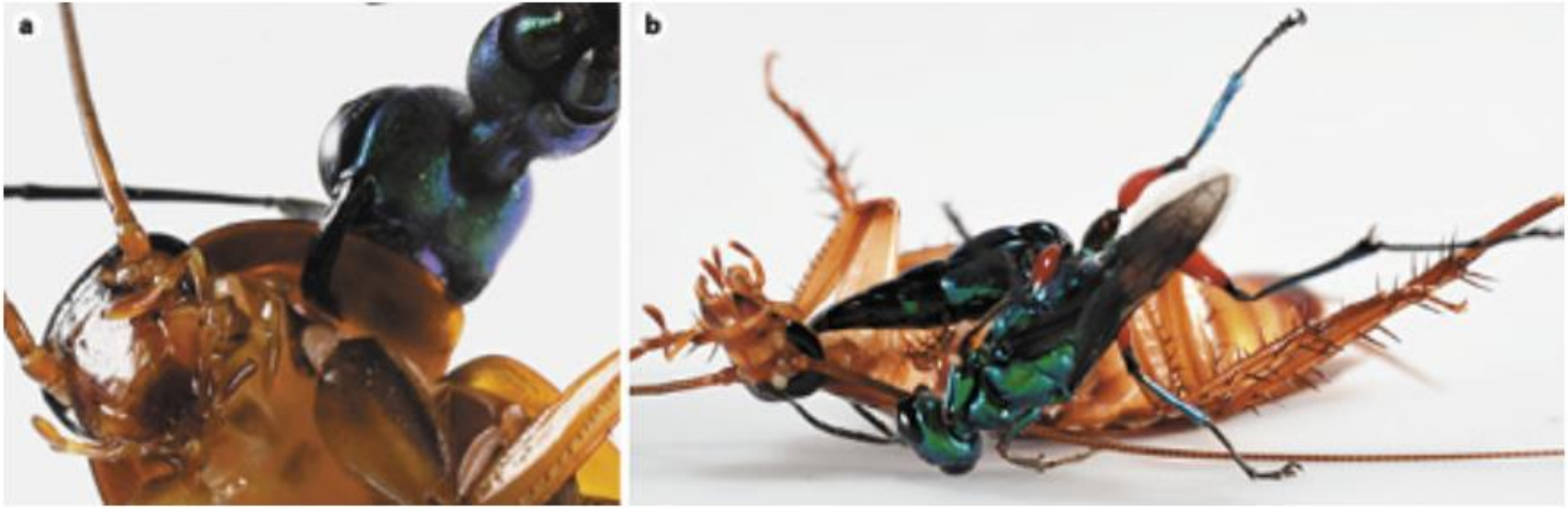
Cockroaches win 50% of the time: Thus, for a cockroach not to become a zombie, the best strategy is: be vigilant, protect your throat, and strike repeatedly at the head of the attacker.

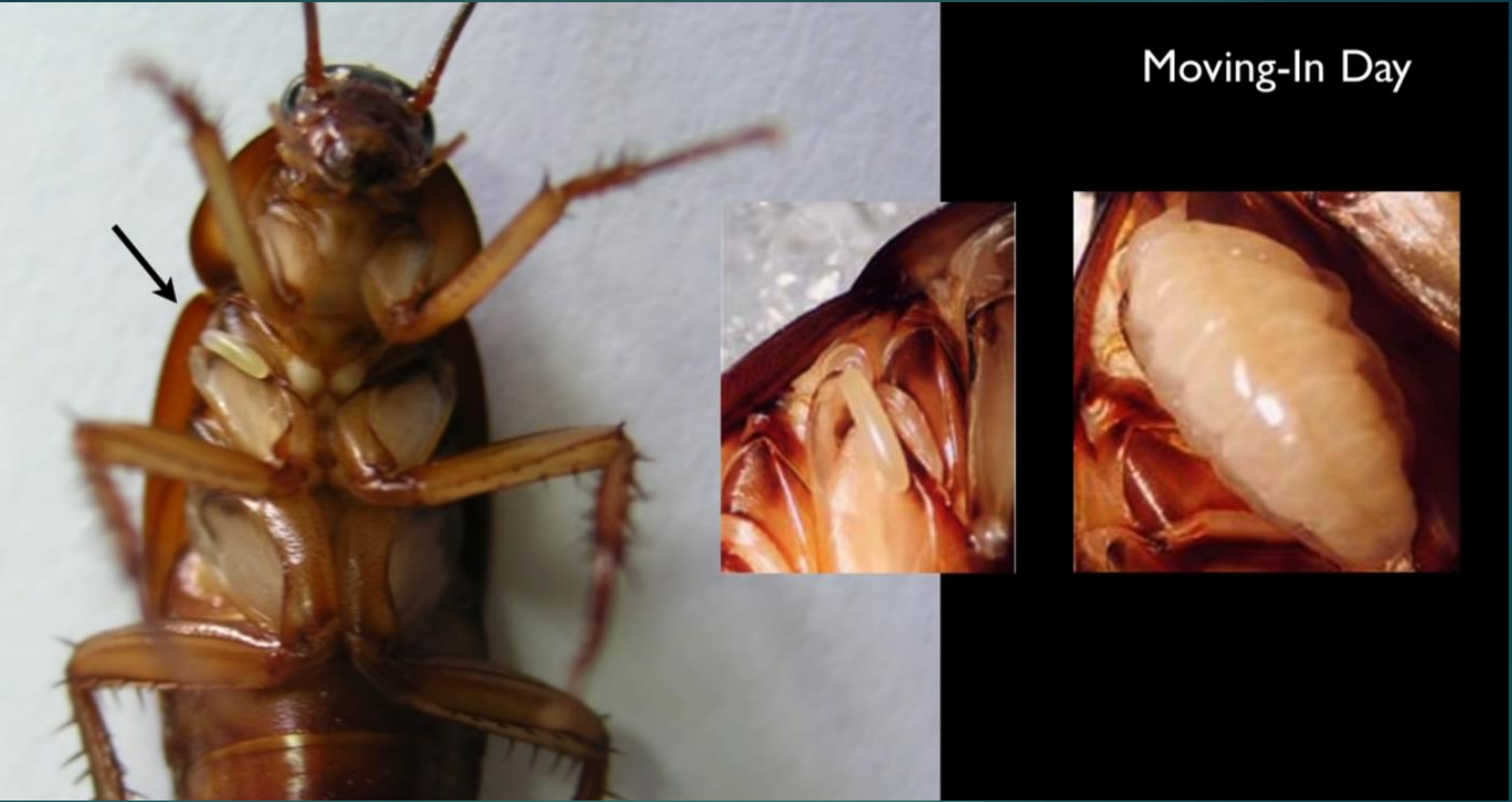
Stings the cockroach. After a minute stands up but cannot move. Now a zombie slave.
Wasp goes and checks on burrow it has dug for 30 minutes. Returns. Roach still there. Grabs it’s antenna, and like dog on a leash, walks it to burrow.

The wasp that always stings twice

Its stinger is a sense organ that can differentiate various brain textures in roach’s brain

Jewel





Puts roach inside pre-dug burrow and lays 1 egg on it and then covers burrow

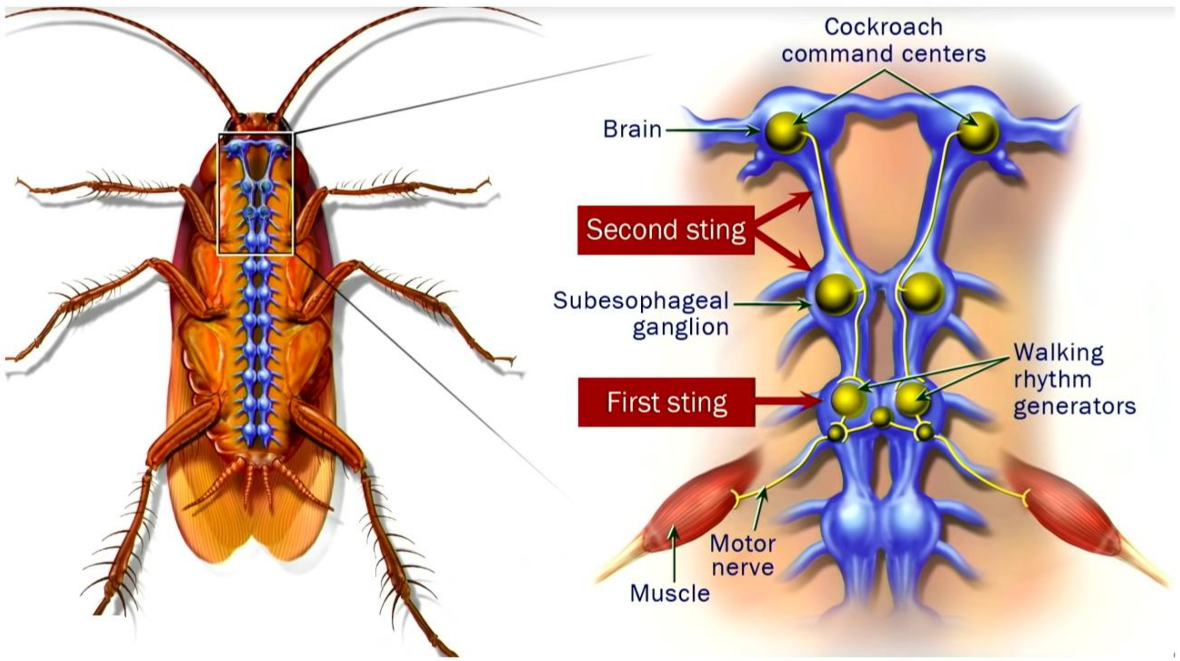
Emerging from terminated cockroach

Wasp finally emerges from it’s cockroach and burrow to go mate. Cycle starts over.

Control of Spontaneity: Use of neurotoxins to “hijack” the decision-making ability of another insect

- The cockroach central nervous system is comprised of two cerebral ganglia in the head.
- CX brain ganglia shows increased firing rates preceding initiation of locomotion and stimulation of the CX promotes walking: CX is necessary for initiation of spontaneous walking, for control of behavioral spontaneity. ‘Cockroach’s free will’
- The Jewel Wasp (*Ampulex compressa*) stings cockroaches (*Periplaneta americana*) and injects venom into the SEG and in and around the CX in the brain.
- The venom induces a 3-7 day hypokinetic state characterized by the inability of the stung cockroach to initiate walking. Other behaviors such as righting, flying, or grooming are not affected.

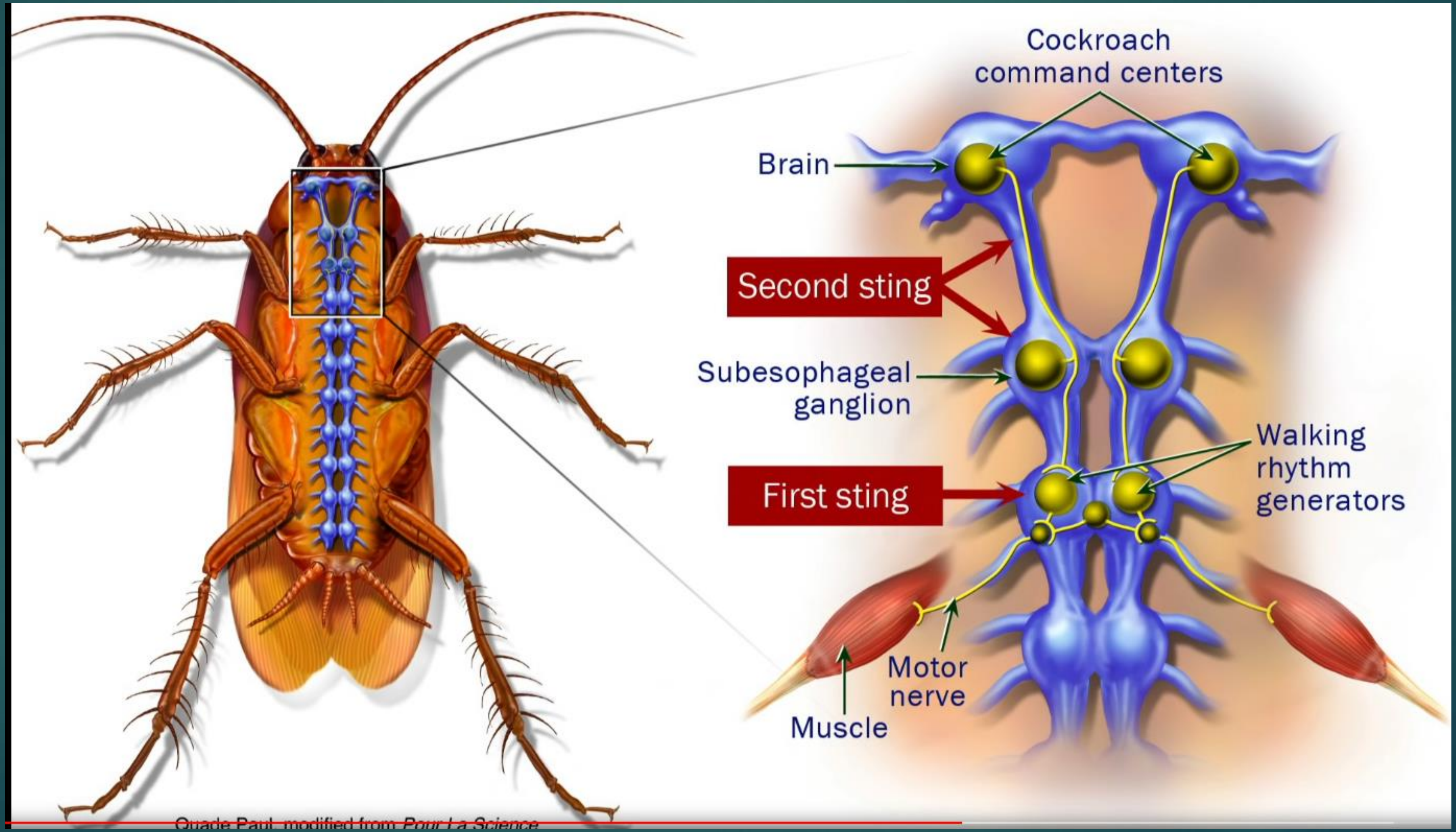
Injections x 2



Carl Zimmer, TEDed Parasite tales. Quade Paul, modified from Pour La Science

Discovery of central pattern generator in locusts in 1950s:, i. e. wing beats, leg coordination; highly conserved from anthropoids to mammals ; 1st injection nixes ability to use front legs

2 precise stings: 1st to walking rhythm generators; for a minute can't move; 2nd to motivation centers

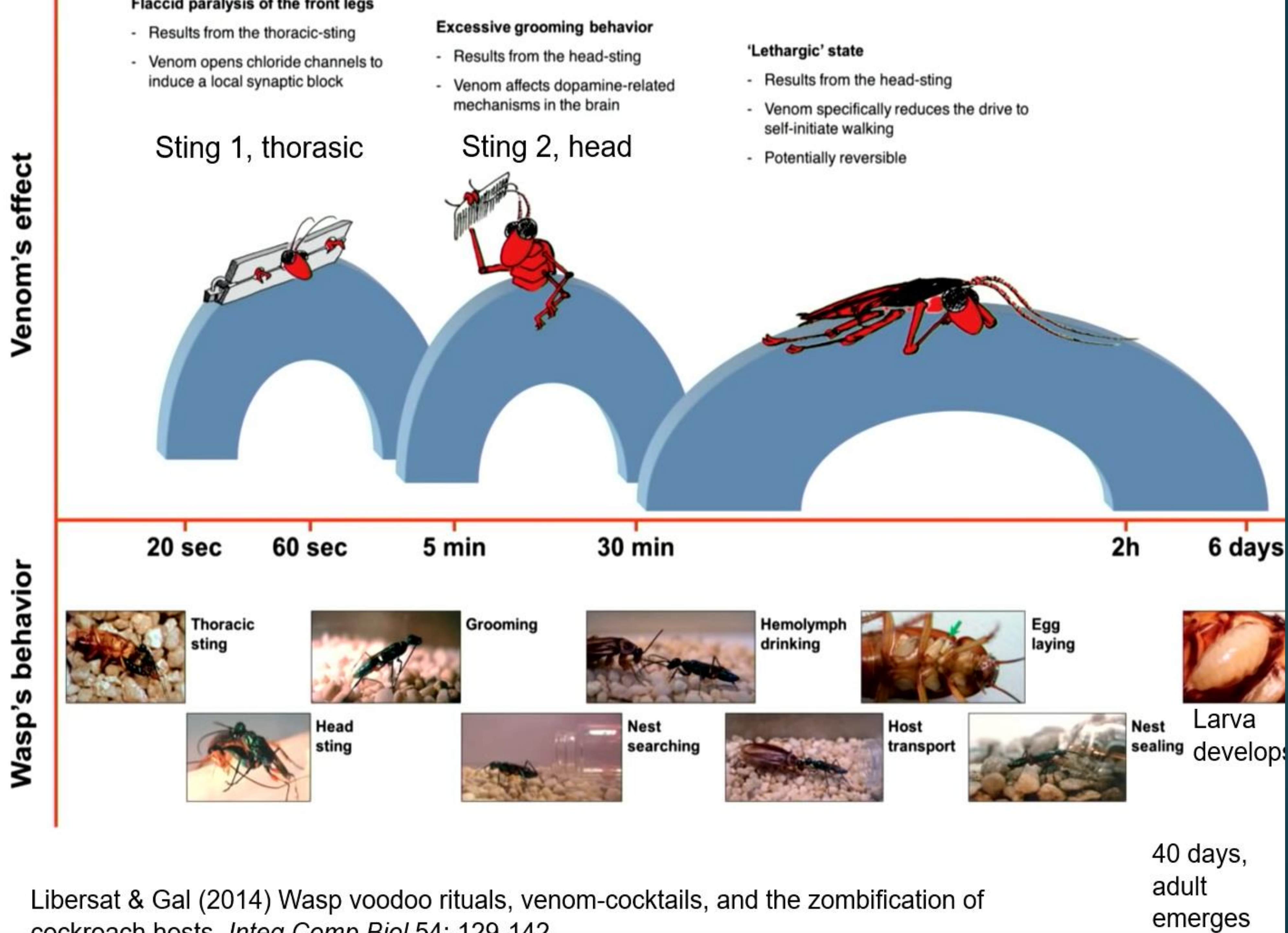


Emerald Jewel wasp (*Ampulex compressa*)

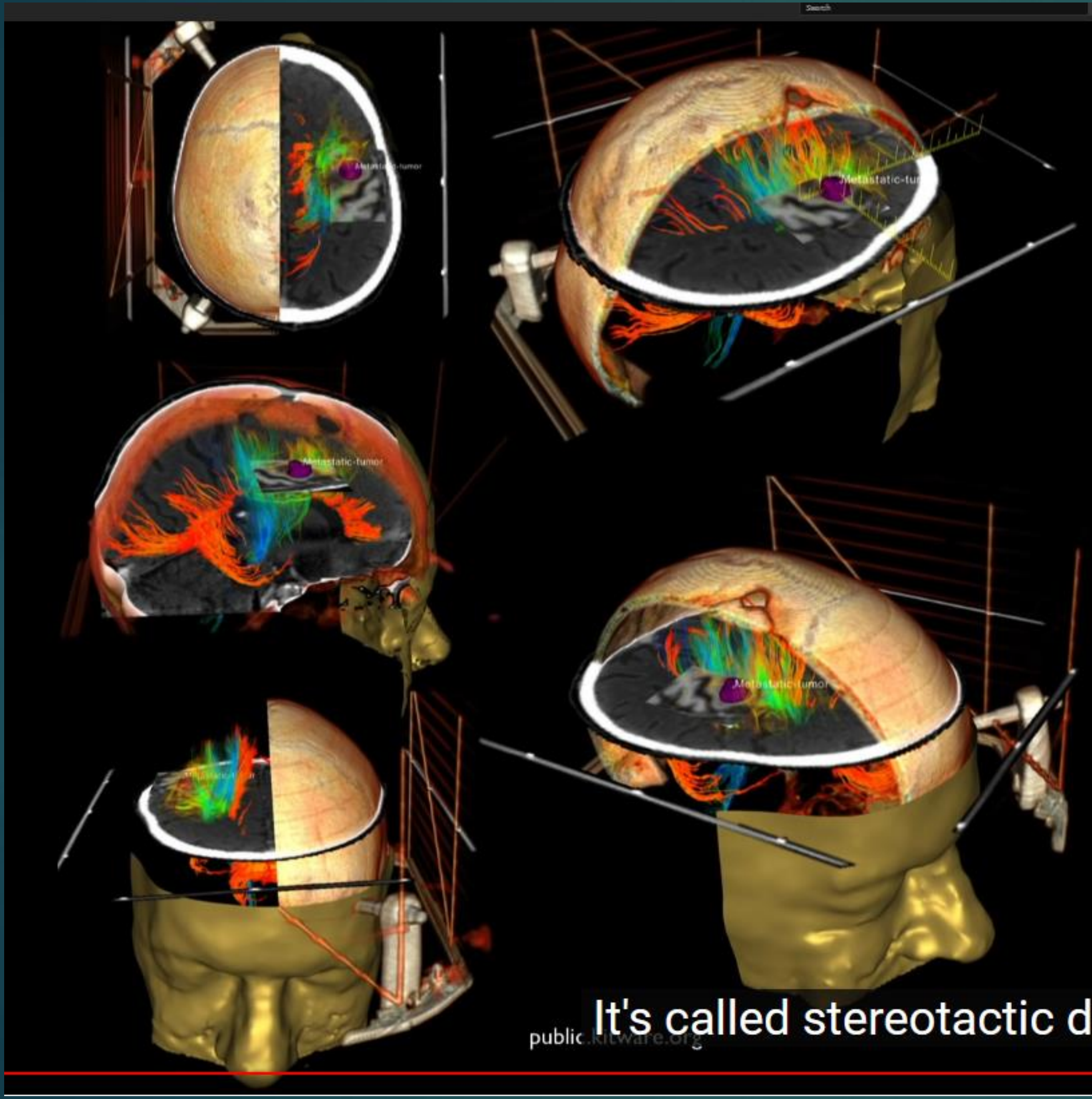
- The wasp stings the cockroach twice: First in the thoracic ganglion (SEG), paralyzing its front legs and enabling the wasp to deliver a second, more difficult sting, directly into the CX ganglia.
- This second sting makes the cockroach groom itself excessively before sinking into a state of hypokinesia – fails to self-initiate walking or escape behaviors.
- The wasp then pulls the idle cockroach into its burrow, like dog on a leash, where it deposits an egg onto its abdomen and buries it for the growing larva to feed on.
- Keeping the cockroach in a hypokinetic state at this stage, rather than simply killing it, allows it to stay "fresh" for longer for the larva to feed on.
- The adult wasp emerges after 6 weeks, leaving behind empty shell.

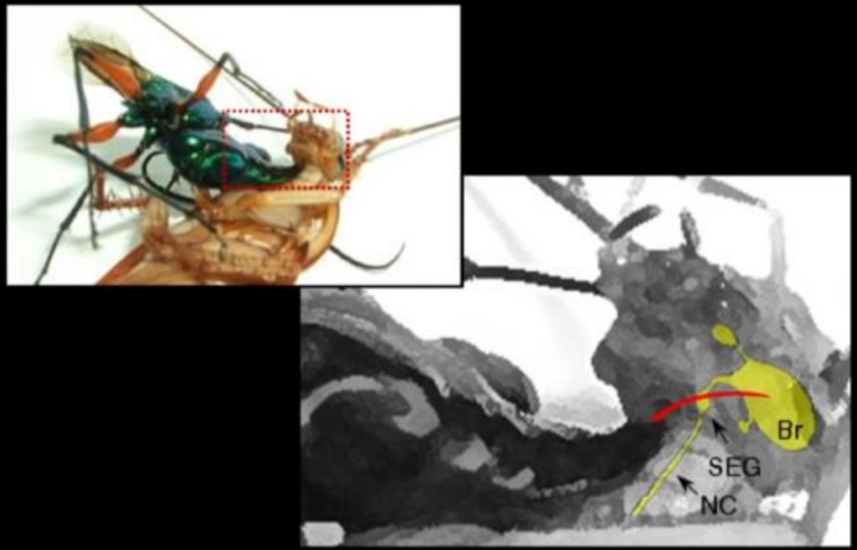
Emerald Jewel wasp

- Unlike most other parasitoids, the is tropical wasp does not simply paralyze its prey to immobilize it.
- Toxin affects not the host's *ability* to move, but its *motivation* to do so. It turns the cockroach into a submissive ‘zombie' unable to self-initiate locomotion. It employs them as live, yet immobile food supply for its larva.
- The cockroach has the ability to walk, run, or fly if properly stimulated, but it does not try to escape as it is slowly eaten alive by the developing wasp larva for 1 month.
- Human relevance: idea of impaired ‘motor motivation’ in Parkinson’s Disease: Nature of free will?



Libersat & Gal (2014) Wasp voodoo rituals, venom-cocktails, and the zombification of cockroach hosts. *Integ Comp Biol* 54: 129-142





It’s harder for us to do:
Requires rigid head gear & MRI

Increases dopamine and increases opioid action

- The head sting induces first 30 min of intense grooming followed by hypokinesia during which the cockroach is unable to generate an escape response. In addition, stung cockroaches survive longer, lose less water, and consume less oxygen.
- Dopamine identified in the venom appears to induce 30 min of intense grooming.
- The opioid system, which is known to affect responsiveness to stimuli in insects, is a target of 2^{nd} sting. Increases opioid effect in CX ganglia.
- Decreasing opioid receptor activity increase startle threshold in control cockroaches. The venom tamps down the activity of neurons that trigger escape response. This effect is reversed with naloxone, an opioid antagonist.

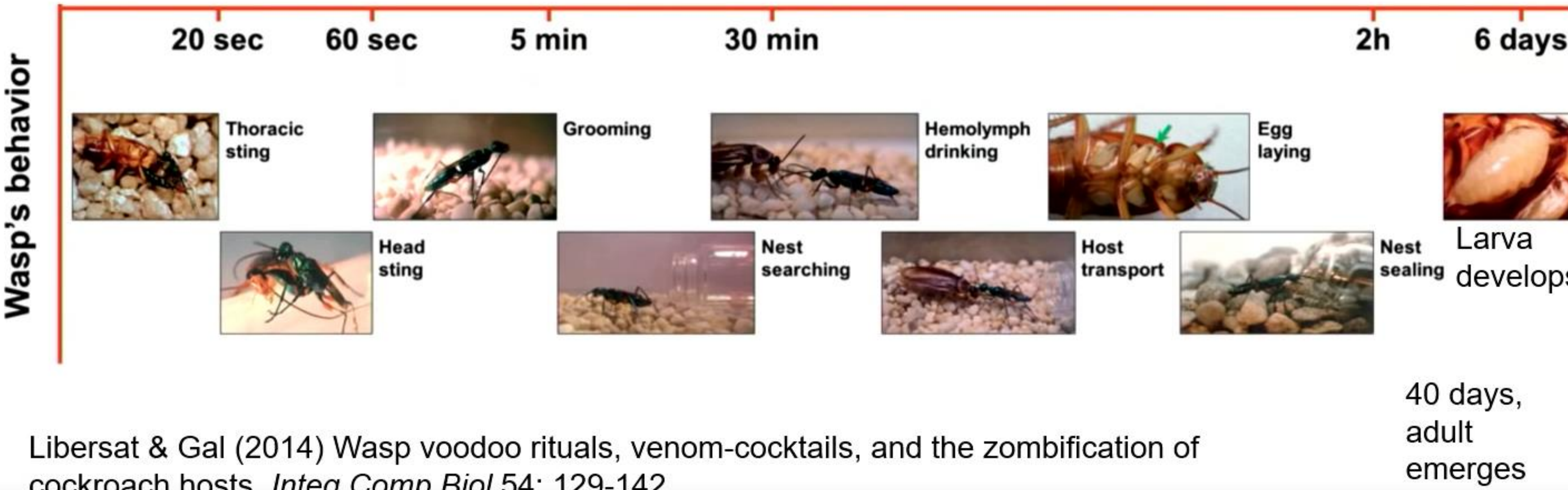
On predatory wasps and zombie cockroaches

Investigations of "free will" and spontaneous behavior in insects

by Ram Gal & Frederic Libersat, 2010

- "To conclude, we hope that by investigating the neuronal basis of such parasite-induced alterations of host behavior, we might further our understanding of the neurobiology of the selection and initiation of behaviors and the associated neural mechanisms underlying changes in behavioral spontaneity. Our results indicate a mechanism which might cut through phylogenetic borders and could form the biological substrate for what we humans experience as "free will"."

Lifecycle: Wasp voodoo rituals, venom-cocktails, and the zombification of cockroach hosts



Libersat & Gal (2014) Wasp voodoo rituals, venom-cocktails, and the zombification of cockroach hosts. *Integ Comp Biol* 54: 129-142.

Potential drug leads …

Head sting venom: > 250 proteins,
including newly found ampulexins and precursors which are only activated once injected, hijacking control of the host's brain by introducing a 'storm' of the host's own neurochemicals.

Long term interest – Parkinson's disease

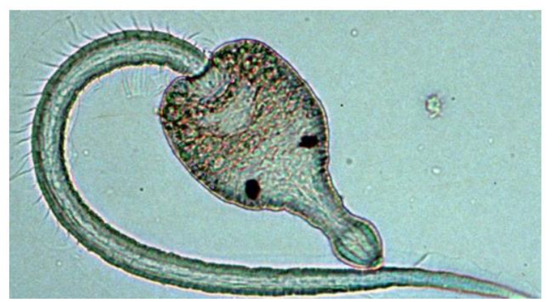
Arvidson et al, (2019) Parasitoid jewel wasp mounts multipronged neurochemical attack to hijack a host brain. *Molecular & Cellular Proteomics* 18: 99.

Moore et al (2018) Ampulexins: A New Family of Peptides in Venom of the Emerald Jewel Wasp, *Ampulex compressa*. *Biochemistry*.

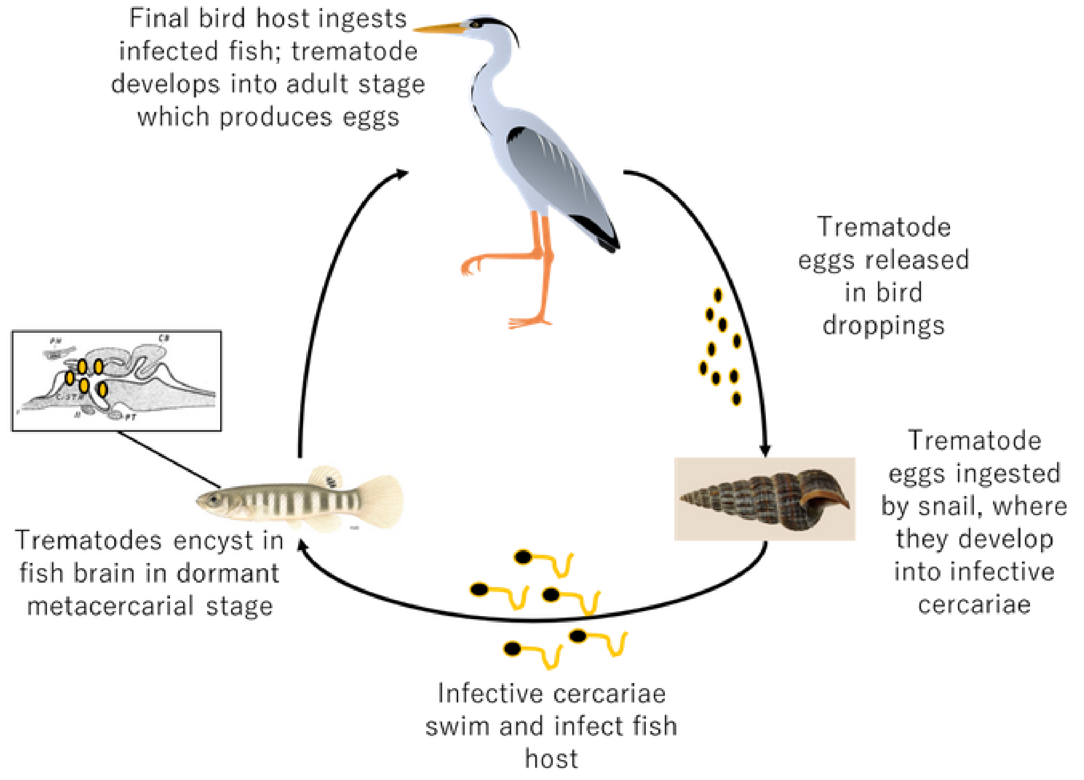
Horror Film


Hornworm
Meets
"Alien"
NortonLifeLock
Denied webcam access to Snagit
View Details

Euthaplorchis Californiensis cycle



- Fluke worm lives in gut of shorebirds; eggs exit in feces
- Eaten by a snail; then escapes from snail
- Shallowed by a killifish; end up in their brain
- Makes fish swim in circles at top of water
- Where they are seen & eaten by a shorebird
- And the cycle starts again



Life cycle of the trophically-transmitted *Euhaplorchis californiensis* trematode. [Source images 1, 2, 3, 4]

Euhaplorchis californiensis

- *Euhaplorchis californiensis* is a tropically transmitted parasite that thrives in salt-water marshes.
- This clever parasite lives in three different hosts, which include Horn snails, shorebirds, and killifish.
- It alters the behavior of the host increasing the odds of moving to the next host.
- The life cycle includes eggs being released in the droppings of the shorebird, then the horn snail consuming the droppings. Once the parasite enters the horn snail it becomes sterile.

Euhaplorchis californiensis

- Once the cercariae develop in the horn snail, they swim out into the marsh and attach themselves onto the gills of a killifish. Killifish normally stay away from the surface of the water to avoid being picked off by wading birds.

- But when they're infected with flatworms known as flukes, they spend more time near the surface and sometimes roll so that their silvery bellies glint in the light.
- Infected killifish are far more likely to be picked off than healthy ones.
- And it just so happens that the gut of a bird is where the flukes need to go next to mature and reproduce

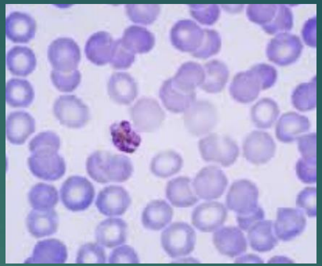
Thorny-headed worm Pseudocorynosoma constrictum & Amphipod Hyalella azteca

- A tiny crustacean, Hyalella azteca, lives in obscurity at the murky bottom of lakes and ponds—unless it's invaded by the larva of a thorny-headed worm.
- When the larva matures, the amphipod abandons its safe dark home and swims toward the light of the surface. For the host, it's a fatal mistake.
- Waiting above are ducks and other waterfowl keen to eat the amphipods as they surface.
- But for the parasite— turned orange by pigments pilfered from its victim's tissue—it's just part of the plan.
- Thorny-headed worms can grow to maturity only in the guts of waterfowl.

Microphallus is a parasitic trematode (fluke): 2 hosts

- *Microphallus piriformes* causes its host, the rough periwinkle snail, to move upwards, making it more vulnerable to predation by herring gulls.
- *Microphallus pseudopygmaeus* chemically castrates (parasitic castration) its host, the snail *Onoba aculeus*, and causes it to grow larger than normal. Castration decreases host energy spent on reproduction
- *Microphallus papillorobustus* causes its host, the lagoon sand shrimp (*Gammarus insensibilis*) to swim upwards, making it more vulnerable to predation

Dieting: *Plasmodium protects the* Mosquito



- Parasites can coax a host to guard them while they're still living inside it.
- Before infecting a human host, *Plasmodium,* the protozoan that causes malaria, first lives in a mosquito.
- The mosquito needs to drink blood to survive. But this behavior poses a risk to the protozoan, because the mosquito may be crushed by the hand of an annoyed human victim, ending the *Plasmodium*
- Goes on diet: To reduce this risk while it is still developing in the mosquito, *Plasmodium* makes its host blood shy, seeking fewer victims each night and giving up faster if it can't find a gusher of blood.

Mosquito

- Once *Plasmodium* has matured and is ready to enter a human host, it manipulates the mosquito's behavior in the opposite direction.
- Now the mosquito grows thirsty and foolhardy, seeking out more humans each night and biting repeatedly even if it is already full.
- At this point, If the mosquito dies at the hand of a human, it is no longer of any consequence. *Plasmodium* has moved on.

Normal snail: eye stalks are hollow

Leucochloridium variae, the brown-banded broodsac worm

- Aggressive mimicry: the parasite vaguely resembles the food of the host; this gains the parasite entry into the host's body.

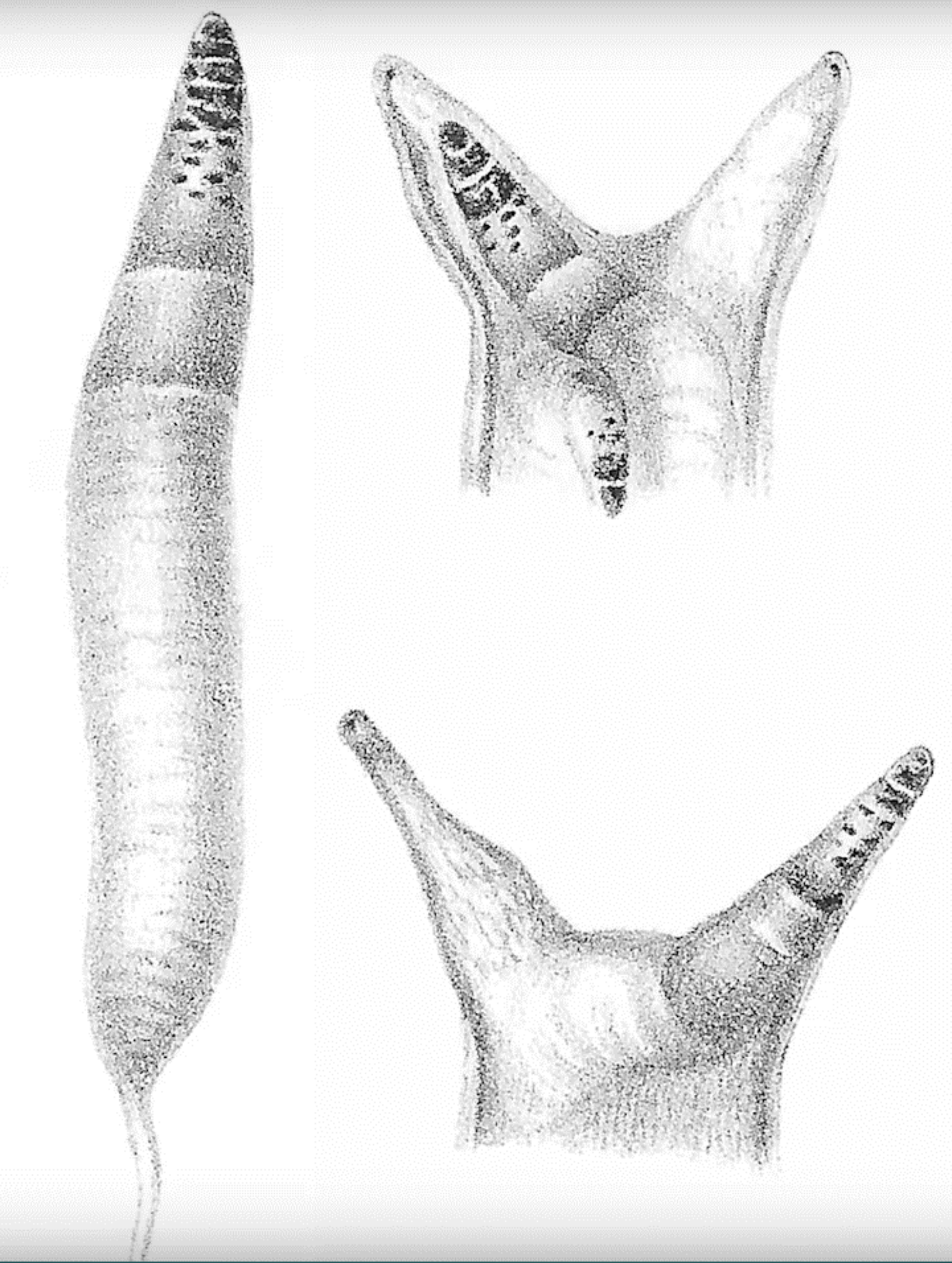
- *Leucochloridium variae:* This parasite invades the eyestalks of snails and make then swollen, pulsating and colorful in order to attract birds. The birds rip out the eyestalks and eat them.

- *Leucochloridium paradoxum* matures inside snails of the genus *Succinea*. When ready to switch to its definitive host, a bird, it influences the normally nocturnal snail to climb out into the open during the day for an increased chance of being consumed by a bird.

Sporocyte

Fluke worm needs a bird to eat it. Solution: Green banded worm broodsac *Leucochloridium* sporocyte pulsates in light, normally shade-loving snail climbs high onto sunny leaf...

Snail eats bird droppings; broodsac turns eye sockets bright green and pulsates 70x a minute, which attracts birds



If you were a bird,
Would this attract
 you?

Why is this caterpillar thrashing? Protecting its siblings?

Insect care of offspring: production of bodyguards

- Although solitary insects are not known to provide care and safety to their offspring, one of the most fascinating behavioral manipulations of parasites is to coerce a host to care for the parasite's offspring.

- Bodyguard manipulation: This manipulation is known in insect parasites and consists in coercing the host in providing protection to the parasite's offspring from predators.

- Protection of this form has been reported for various caterpillar-wasp associations.

Glyptapanteles wasp & *Thyrinteina leucocerae* caterpillar.

- Wasp injects eggs into caterpillar. The caterpillar quickly recovers from the attack and resumes feeding. The wasp larvae mature by feeding on the host, and after 2 weeks, up to 80 fully grown larvae emerge from the host prior to pupation.
- One or two larvae remain within the caterpillar while their siblings perforate the caterpillar body and begin to pupate. After emergence of the larval wasps to pupate, the remaining larvae take control of the caterpillar behavior by an unknown mechanism, causing the host to snap its upper body back and forth violently, deterring predators and protecting their pupating siblings.
- Un-parasitized caterpillars do not show this behavior. This bodyguard behavior results in a reduction in mortality of the parasitic wasp offspring.

Glyptapanteles wasps discovered a form of babysitting millions of years ago

Parasitized caterpillars become true bodyguards/babysitters; will trash around if any creature comes close to cocoons

A cabbage butterfly caterpillar stands watch over white butterfly wasp cocoons, a common parasite that kills its caterpillar hosts by eating them from the inside out.

Cotesa glomerata wasp and cabbage butterfly caterpillar

Cotesa glomerata wasp: lays 60-80 eggs

Warning: Nature’s horror video

Larva know how to avoid vital organs of host

Poor caterpillar

Come out by the dozens and spin silken cocoon

Amazingly the caterpillar survives

A few larva stay behind in caterpillar, releasing chemicals that continue brain control. It adds its own layer of its own silk to cover the brood. It then bats away any predators. Fends off 58% of predators.

Caterpillar protects wasp cocoons until it starves to death

Male wasps emerge first and wait for females.

70% of white caterpillars suffer this fate

Evolutionary reason: To prevent hyperparasitic wasp from injecting eggs into wasp cocoons

Does protection work?
yes, hyper-parasitism reduced by 50% if caterpillar 'guarding'

You get your comeuppance…

- *Cotesia glomerata* is in turn parasitized by the hyperparasite wasp *Lysibia nana*.
- Female Lysibia are attracted to plants that have been attacked by caterpillars infected by *C. glomerata*.
- Once a suitable host has been found, the *L. nana* female lays an egg in a *C. glomerata* larva.

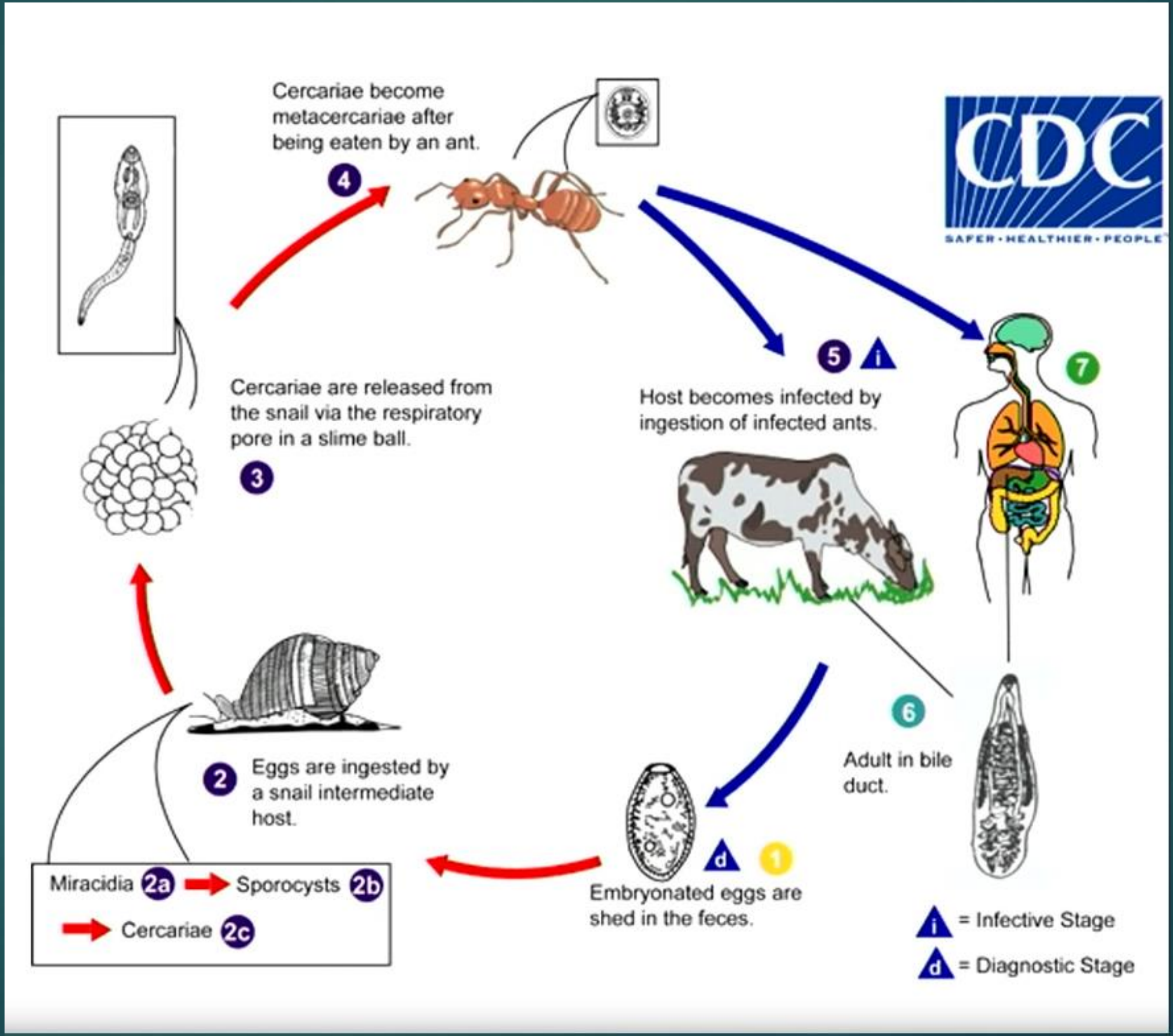
Guardian Ants: Caterpillar enslaves ants

- Fat and juicy caterpillar are a tempting snack for many predators
- The caterpillars of the Japanese oakblue butterfly (Narathura japonica) grow up wrapped inside leaves on oak trees. To protect themselves against predators like spiders and wasps, they attract ant bodyguards, Pristomyrmex punctatus, with an offering of sugar droplets
- The caterpillar secretes a sweet, sticky substance that alters the ants so that they will aggressively attack anything threatening the butterfly larvae.
- The sugary droplets do not bribe the ants into providing protection to the caterpillar. New research has revealed the secretion actually changes the brain chemistry of the ants so they neglect their own colony in favor of the caterpillar.

Caterpillar-ant cooperation not mutualistic.

- Ants who drank the secretions had lower levels of dopamine in their brains.
- This seemed to result in the ants being less active and exploring around less.
- The insects became significantly more aggressive when the caterpillar showed signs of alarm, such as retracting its tentacles.
- So rather than providing a reward to the ants in exchange for their protection, the caterpillars are actually enslaving them.

Lancet liver fluke (*Dicrocoelium dendriticum*)

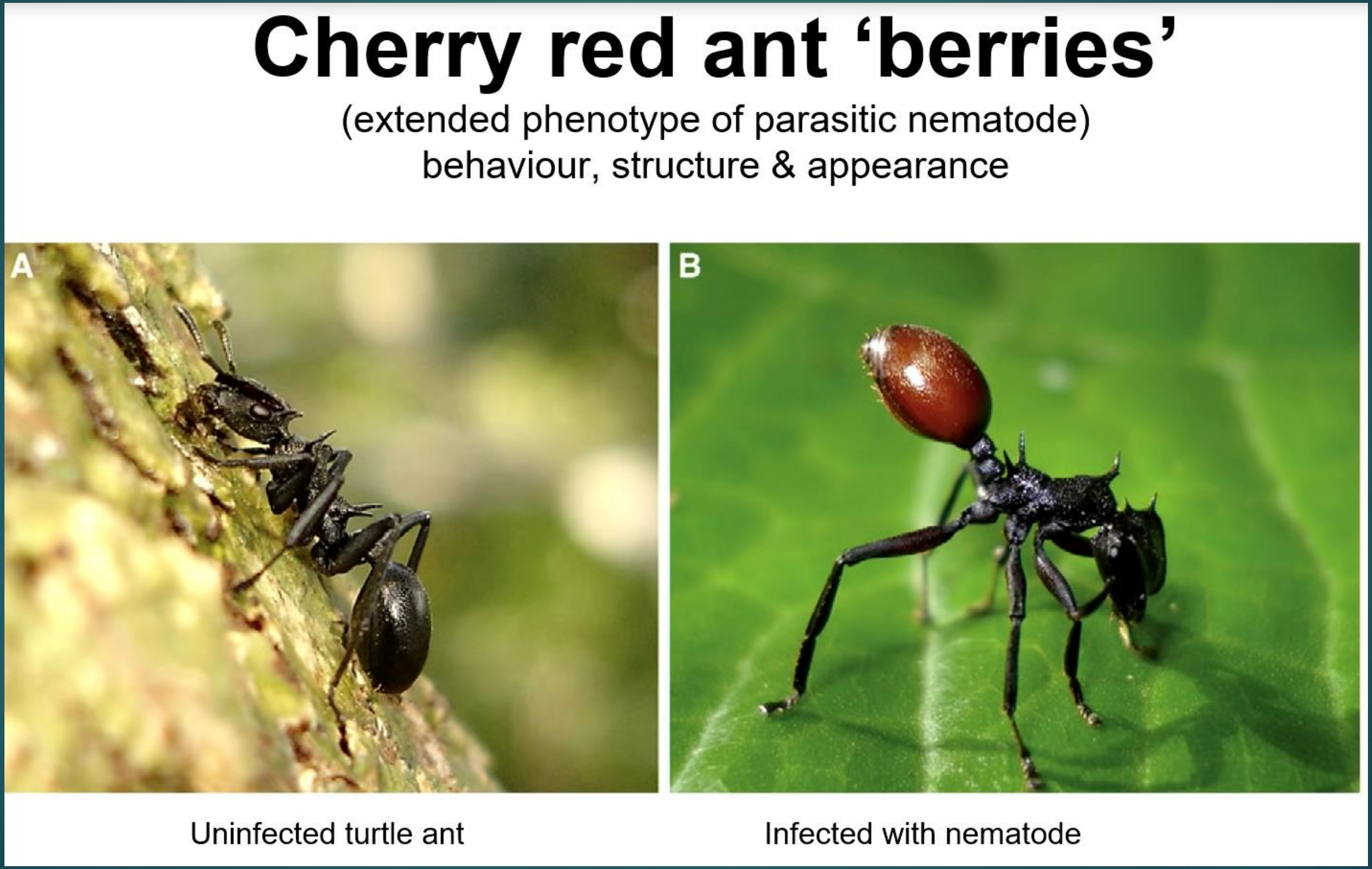


Lancet liver fluke (*Dicrocoelium dendriticum*) & ant (*Formica fusca*)

- Snail then to intermediate host (the ant) to the final host (liver of a grazing animal).
- Snail eats feces of animal. Ant uses the trail of snail slime as a source of moisture. Ant eats slime ball of snail. Fluke takes over the ant's navigational skills to coerce it into climbing to the tip of a blade of grass. In early evening, ant leaves colony, climbs up grass, bites stem at top. If not eaten by cow by morning, climbs down and rejoins colony, repeat!

Hohorst and Graefe, 1961

If you are a nematode that needs to attract a bird, turn your ant into a berry high up in canopy



Come and eat me!

- Bird droppings gathered by the arboreal ant Cephalotes atratus can contain a hidden menace: the parasitic nematode Myrmeconema neotropicum.

- Once inside the ant, the nematode turns its host's abdomen maroon, so that it mimics a ripe berry attractive to birds. To make its unwitting host even more enticing, the nematode induces the ant to walk with its abdomen raised

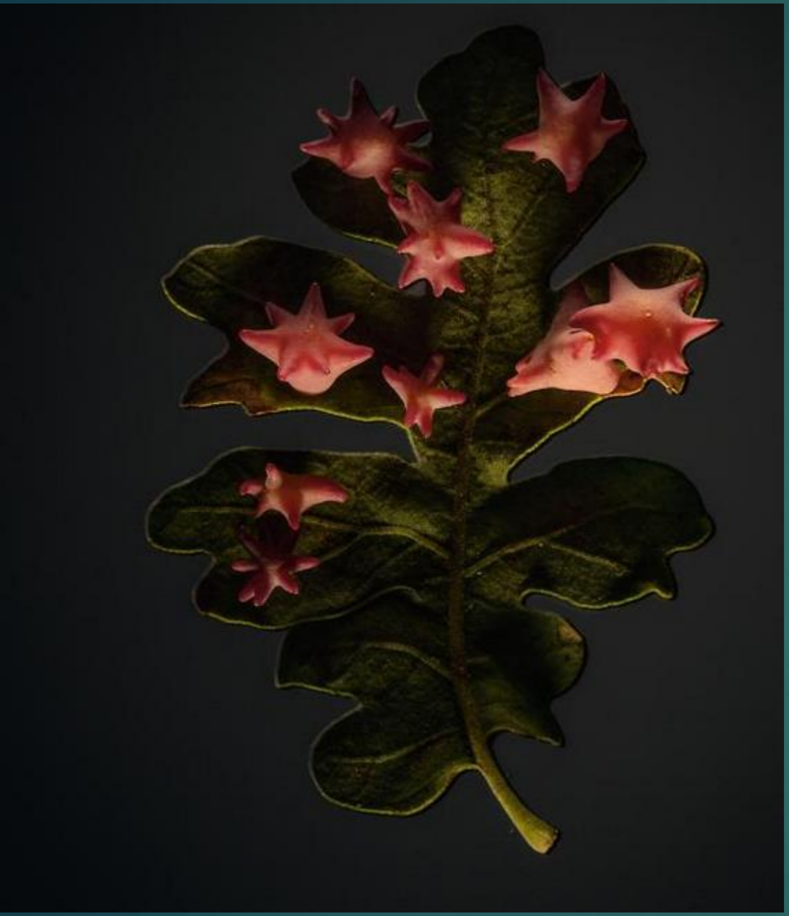
Baculovirus: wilting disease

- Baculoviruses infect the caterpillars of gypsy moths and butterflies.
- On the outside the caterpillar appears normal, continuing to munch on leaves as before. But the food it eats is not becoming more caterpillar tissue. Instead it's becoming more baculoviruses.
- When the virus is ready to leave its host, the caterpillars undergo a radical change. They become agitated, feeding without rest. And then they begin to climb, remaining on top of leaves or on tree bark in daylight hours, when they are easily seen by predators.
- Certain virus genes become active in caterpillar cells, producing a torrent of enzymes that dissolve the animal into goo (thus "wilting disease"). As the caterpillars dissolve, clumps of viruses shower down onto the leaves below, to be ingested by new caterpillar hosts.

Baculovirus: single gene to control climbing

- The climbing behavior of the caterpillars is an exquisite example of an extended phenotype. By causing their hosts to move up in trees, the baculoviruses increased their chances of infecting a new host down below. To test Dawkins's idea, study examined the genes in baculoviruses, to see if they could find one that controlled the climbing of caterpillars.
- If shut down a single gene in the virus, called *egt*, it continued to infect caterpillar cells and replicate as before, even turning the caterpillars to goo as before. But baculoviruses without a working copy of *egt* could not cause the caterpillars to climb trees.

Plant parasite: Oak Gall



When the spiny turban gall wasp injects its eggs into oak leaves, it leaves behind something extra: a cocktail of chemicals that induces the plant to build pink structures around the growing wasp larvae, called galls. Safely cocooned, the larvae feed on the plant's nutrients. How galling.

Native Americans used these galls to make ink used as hair dye, basket coloring, and tattoo ink.

Plant parasite: Crypt gall wasp (*Bassettia pallida*): 100 species

- Crypt gall wasp parasitizes oak trees. It lays an egg in the stem and larva induces the development of a ‘crypt’ within growing stems.
- Crypt galls are like in-law apartments for parasites.

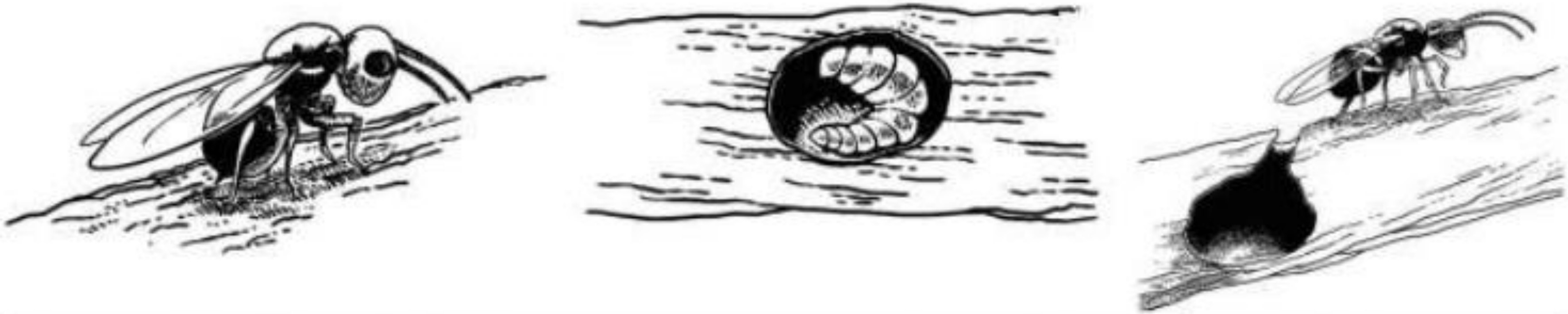
- Has its own hyper-wasp: crypt-keeper wasp (*Euderus set*). Parasitizes 305 different gall wasps from six different species

- Induces adult gall wasp to dig an exit hole in that is too small & they plug the hole with their head and die.
- The hyperparasite then can chew out through softer head rather than tough tree.

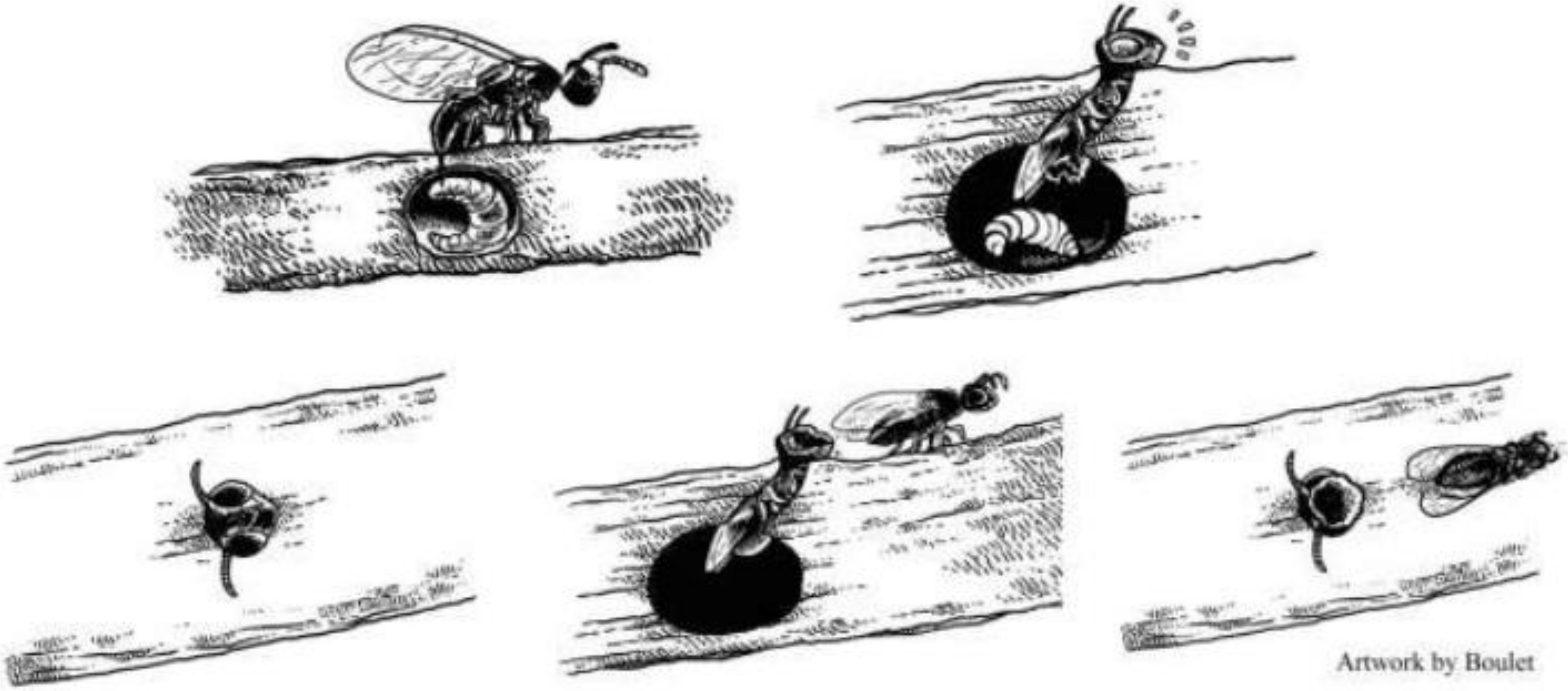
Weinersmith et al., 2017

The crypt-keeper and its victim

A healthy gall wasp matures in a crypt formed in an oak tree and tunnels its way to freedom through the tree's bark.



Euderus set manipulates the gall wasp into making and plugging a tunnel. The parasite bursts out of the crypt through its head.



Artwork by Boulet

Easier way to get out of an oak tree gall

Bassettia pallida, the parasitic wasp that infests oak trees and is itself parasitized by the crypt keeper wasp. Andrew Forbes/University of Iowa

Crypt keeper wasp

Crypt keeper wasp seeks victims based not on their kind but on the vulnerability of their home; prefers galls that were small, smooth, non-woody, lacking fuzz or sharp spines — defenseless

The head of an oak gall wasp, which was parasitized by a crypt-keeper wasp. Anna

Parasitic Love Vines: Feed on Parasitic Wasps That Feed on Trees

Belonocnema treatae, the oak leaf gall wasp. Andrew Forbes

Oak tree galls — compartments of plant tissue containing wasp larvae — with a parasitic vine attached by tiny wooden suction cups. Brandon Martin/Rice University

1 -Parasitic insect (Belonocnema treatae, the oak leaf gall wasp) feeds on a
2 - host plant (sand live oak),
3 - which in turn is feed on by a parasitic plant (love vine, Cassytha filiformis)
4 - Oak galls can have up to five levels of parasitism

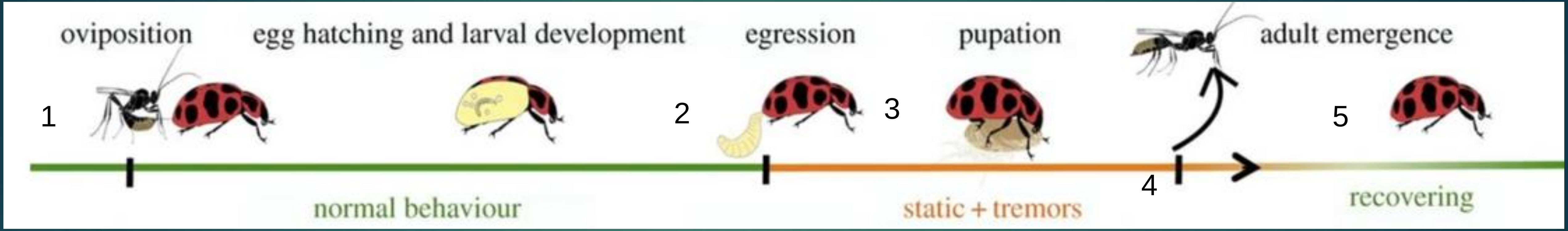
A closer view of the suction cups which the parasitic love vine uses to attach itself to the galls. Scott Egan and Matt Comerford/Rice University

Parasitic *Dinocampus coccinellae* wasp

Parthenogenetic species: all female, clone itself; no mating or fertilization needed


NATIONAL GEOGRAPHIC
REAL ZOMBIES
The Strange Science of the Living Dead

"Who is the puppet master? Replication of a parasitic wasp-associated virus correlates with host behavior manipulation." : life-cycle of the ladybug-preying *Dinocampus coccinellae*



- 1 -Wasp lays its eggs in a ladybug & the larvae develop inside its body
- 2 - 20 days later, a single prepupa egresses and spins a cocoon between the ladybug's legs; An RNA virus in the host's brain tissue triggers paralysis and tremors. This virus may be the real puppet master within.
- 3 - Throughout parasitoid pupation, the host remains alive and positioned on top of the parasitoid cocoon, serving as a zombie bodyguard to prevent predation; 65% protection.
- 4 - After a week, the adult emerges from the cocoon.
- 5 - Some ladybugs recover, resume feeding and can even reproduce.

Viral Puppet master of puppet

- It appears this wasp injects both an egg and a virus.
- Just before the larva exits the host to pupate (and benefits from the bodyguard behavior), it experiences a massive increase in viral replication which are transmitted to the ladybug.
- The virus replication in the host's nervous tissue induces a severe neuropathy and antiviral immune response that correlates with the motor twitches that serve to protect the pupa.
- Hence, the virus is apparently responsible for the behavioral change because of its invasion of the ladybug's brain and the virus clearance correlates with behavioral recovery of the host.

Dheilly et al., 2015

7 day Bodyguard

Ladybug guarding a *Dinocampus coccinellae* cocoon. The ladybug will remain stationary until the adult wasp emerges from its cocoon, and die some time afterwards

Ladybug guarding a *Dinocampus coccinellae* cocoon.
The ladybug will remain stationary until the adult wasp emerges from its cocoon, and die some time afterwards

Plant defenses

- How does *C. glomerata* itself find its hosts? Most parasitoid wasps use scent to sniff our their hosts.
- When attacked by herbivores like caterpillars, plants emit volatile chemical signals call kairomones that acts like a dinner bell for parasitoid wasps.
- Feeding by different species of caterpillars elicit different chemical emissions from the plant
- Wild cabbage plants responded when they come under attack by two different species of caterpillar - *Pieris brassicae* and *P. rapae*. They found that two caterpillars induce very different blends of chemical volatiles from the plant. Plant recognizes them from their saliva chemistry.

For hyperparasitoids, it's what's inside that counts.

- But it is a different story when those caterpillars are parasitized by *C. glomerata*. The physiological alteration that the parasitoid imposed on their host was reflected in how the caterpillar's food plant responded.
- *Cotesia glomerata* manipulated their hosts to such a degree that once parasitized, both *P. brassicae* and *P. rapae* elicited a far more similar blends of chemical emissions from the plant.
- This is where the hyperparasitoid *L. nana* comes in.
- To *L. nana*, whether those caterpillars had parasitoid babies onboard is far more important than their species identity, and they showed no clear preference for either caterpillar species as long as they were parasitized by *C. glomerata*.
- So *C. glomerata* leaves a calling card to their own hyperparasitoids.

Plant defenses: specific plant odors for specific pests

- Many parasitoids are attracted most by plants currently under insect herbivore attack.
- This response is mediated by volatiles produced by the action of the host feeding on the plant.
- Eggs of insect pests deposited on plants trigger the production of scents by plant. Butterfly egg deposition triggers highly specific chemical and structural changes in the plant that attract different parasitic wasps which then attack either butterfly eggs or caterpillars.

Plant defenses: the enemy of my enemy is my friend

- Plants "call for help" to bodyguards that serve to boost plant fitness by limiting herbivore damage. This, by necessity, assumes a three-trophic level food chain.
- When damaged, many plants release hydrocarbons called volatile organic compounds, similar to the compounds that cause the characteristic smell of freshly cut grass.
- These volatile organic compounds, based on unique saliva of specific caterpillars, are known to be attractive to parasitoid wasps that lay their eggs inside other insects, killing them.
- Plants appear to use this strategy to fight back against herbivorous insects by calling for their enemies' enemy
- Herbivorous insects tend to avoid the herbivore-induced volatile organic compounds.

Then the moth

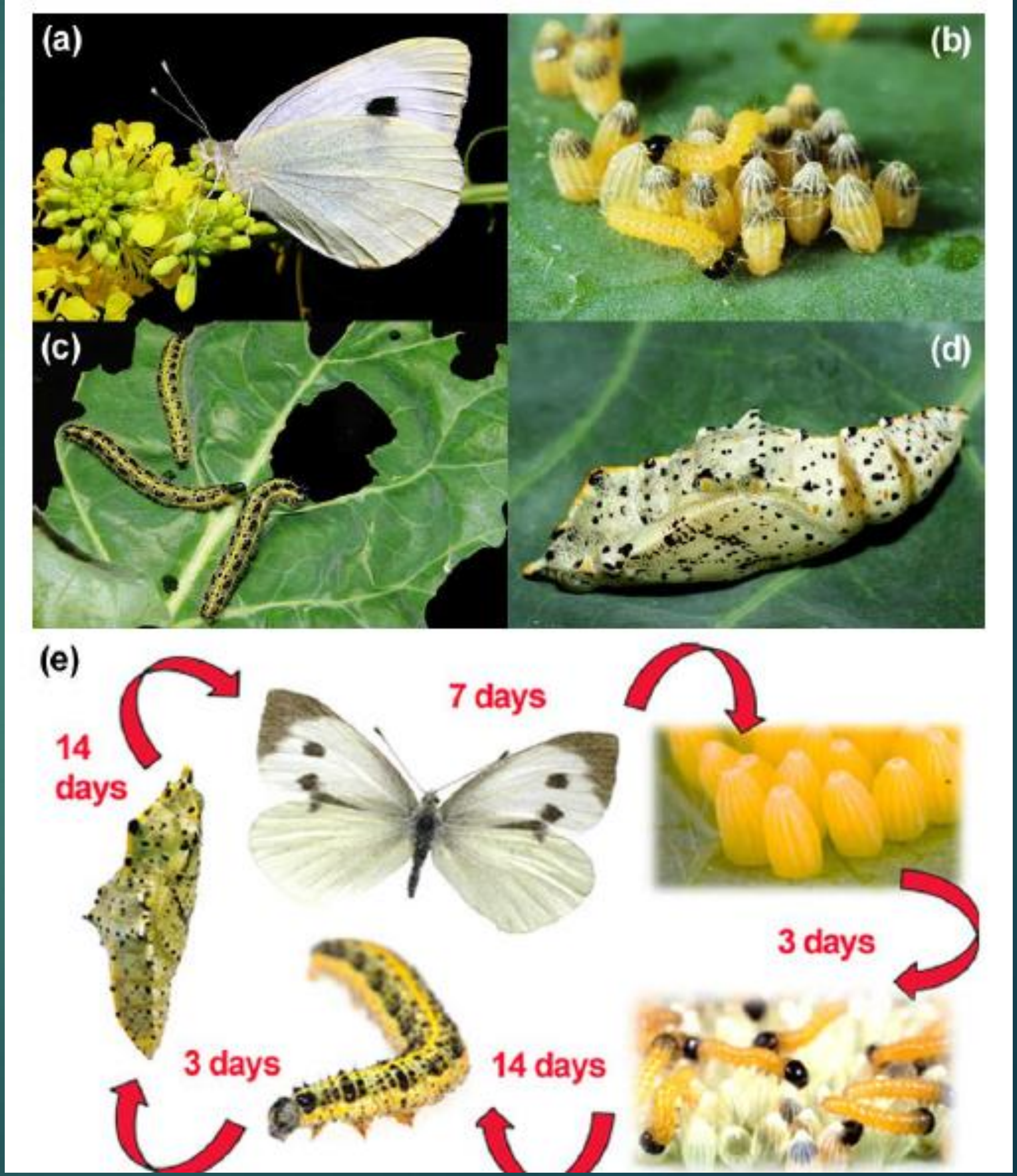
- Cabbage plants eaten by cabbage white caterpillars are particularly attractive to female diamondback moths in search of a plant on which to lay their eggs.
- However, if the caterpillars have been colonized by parasitoids, the plants become less attractive to the diamondback moths. The level of impact depends on the species of parasitoid that is developing within the caterpillars.
- So parasitization is a form of biological control of major pest.

Black mustard (*Brassica nigra*) plant

Brassica nclude turnip (*Brassica rapa*), cabbage, broccoli, cauliflowers (*Brassica oleracea*),

Its enemy = Large White cabbage butterfly (*Pieris brassicae*)

- Butterflies of *P. brassicae* can feed on *B. nigra* mustard plant floral nectar and then oviposit on the lower side of leaves, in batches of 50-100 eggs. After hatching, neonate (first instar) caterpillars move gregariously and feed on leaves.

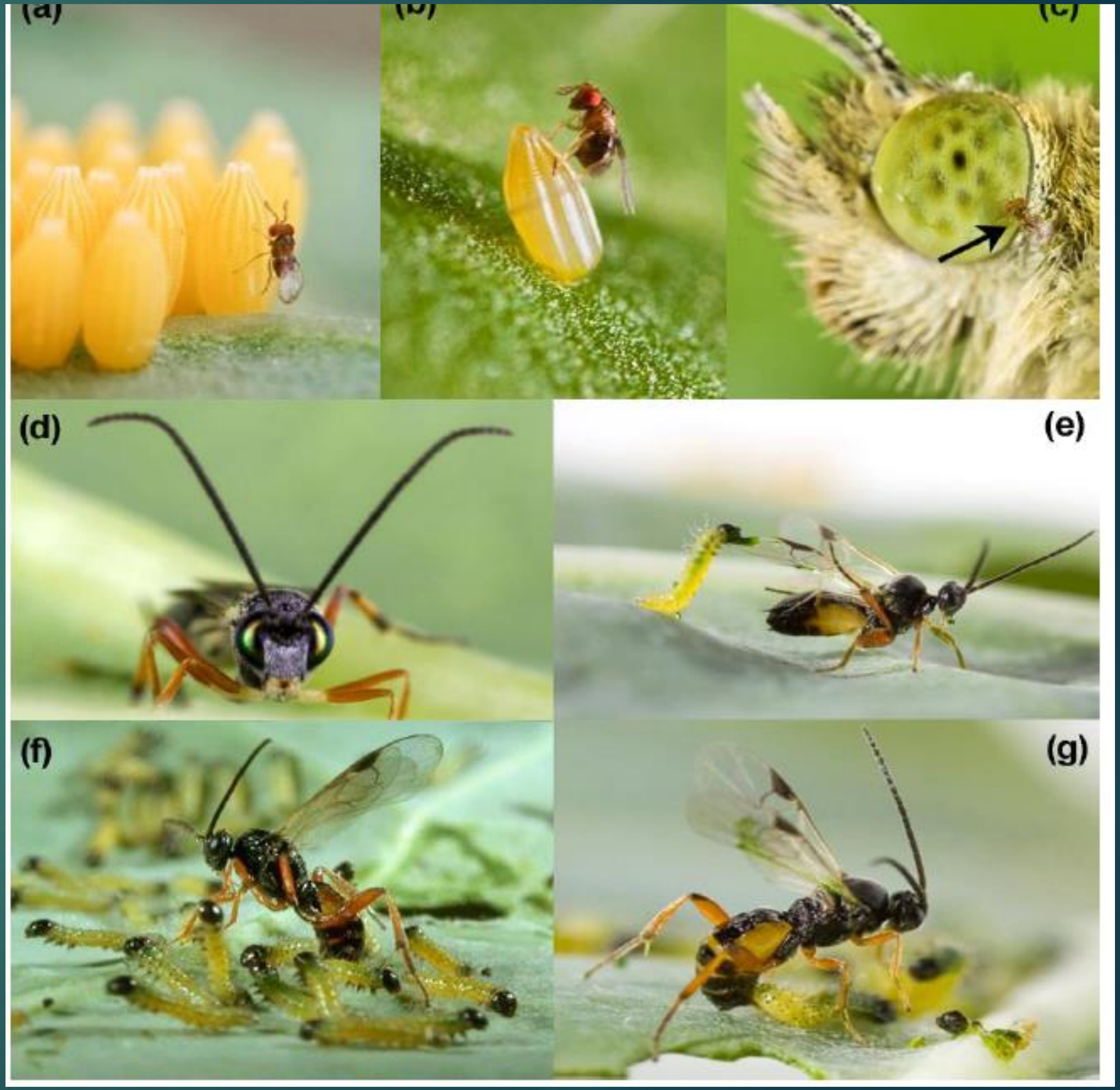


Plant attracts 2 hyperparasites of this caterpillar: enemies of my enemy

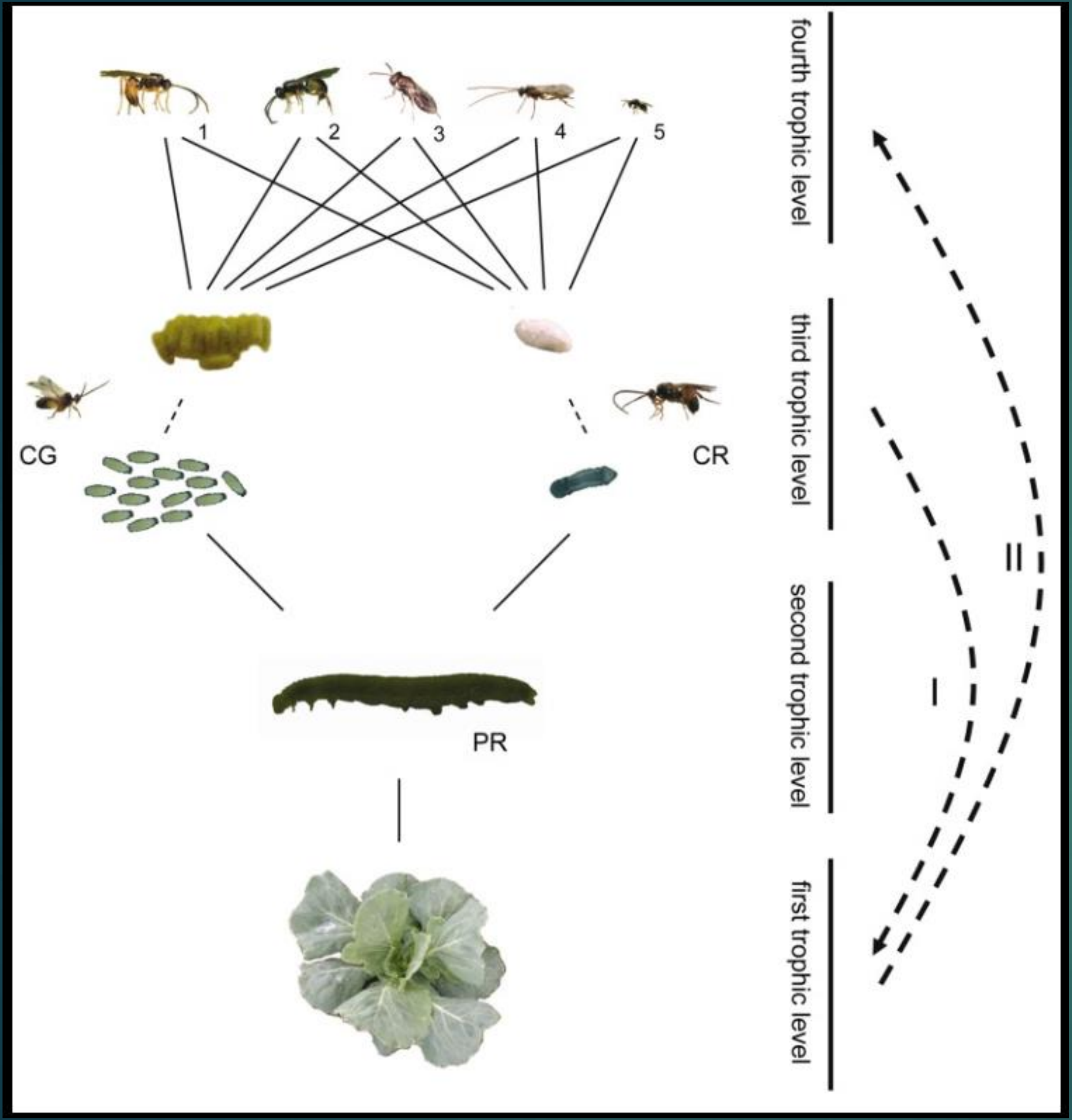
Plant defenses. Parasitoid wasps are attracted by *B. nigra* plant. Plant responds differently to egg deposition by the two lepidopteran species

(a,b) Parasite *Trichogramma brassicae* is attracted by chemical modifications on the leaf surface and lays its eggs inside *P. brassicae´s* eggs.

(d) *Cotesia glomerata also* is attracted by volatiles released upon herbivore damage and attacks early instar of *P. brassicae* **(e-g)** caterpillars to lay eggs.



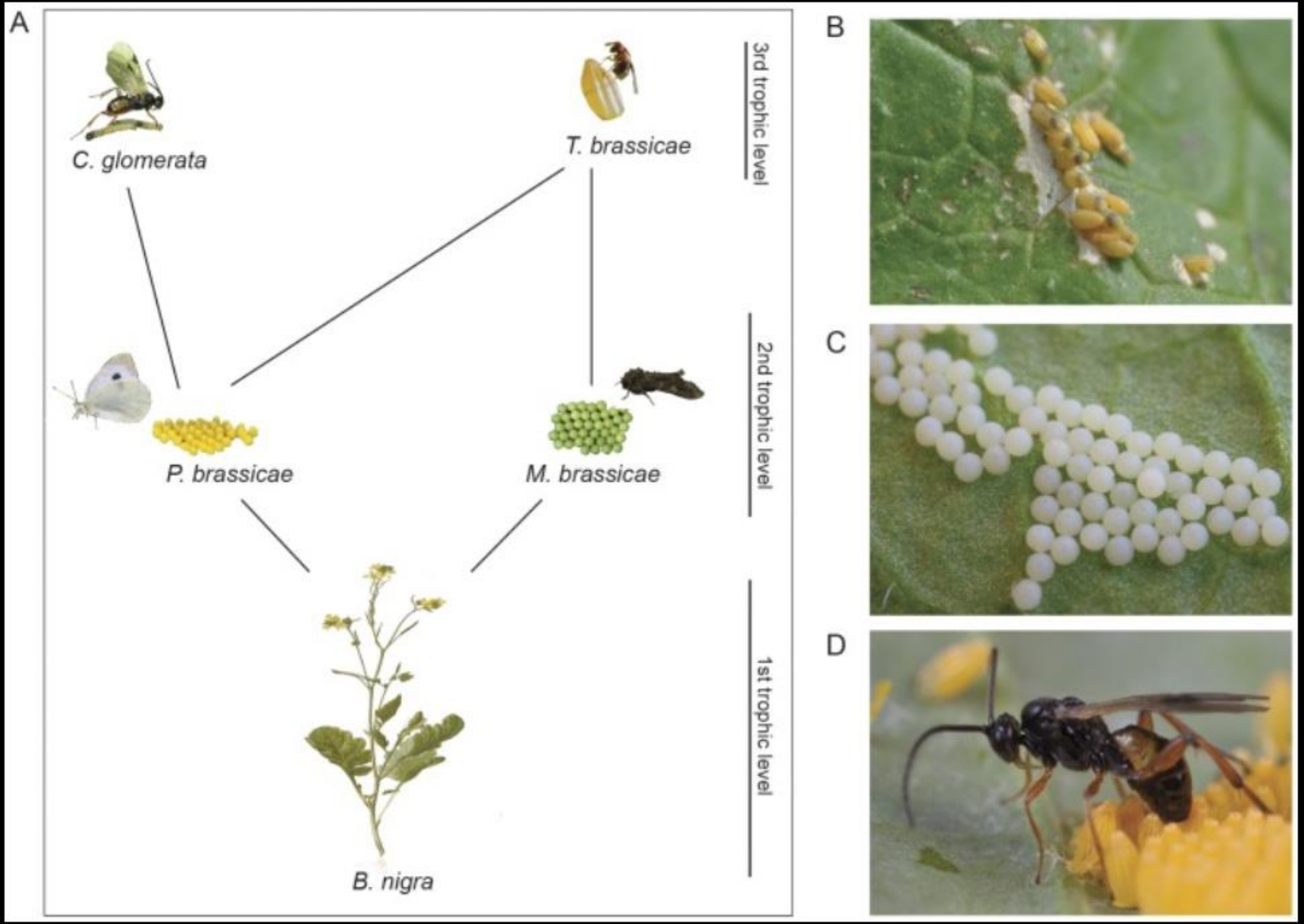
Cotesia glomerata



A food chain is a succession of organisms that eat other organisms and may, in turn, be eaten themselves.

The **trophic level** of an organism is the position it occupies in a food web.

The trophic level of an organism is the number of steps it is from the start of the chain


A
C. glomerata
T. brassicae
3rd trophic level
P. brassicae
M. brassicae
2nd trophic level
B. nigra
1st trophic level
B
C
D

Parasitic wasps are genetically modifying butterflies: Inject a virus that alters the caterpillar's genome

- The wasps inject a virus into the caterpillars along with their eggs. The virus integrates into caterpillar's genome along with some wasp DNA
- Part of an 'arms race' between caterpillars and wasps
- Pieces of DNA from a virus carried by parasitic wasps have become incorporated into the genomes of the butterflies they attack.
- However, over time wasp DNA has also made it into the genomes of butterflies – perhaps from occasions when caterpillars have survived such attacks.
- Discovery that this DNA has actually brought benefits to butterflies by protecting them against other lethal viruses.

Horsehair worm larva

Made the mistake of eating a horsehair worm, which needs to be in water for its next cycle

If you need to get into water to reproduce, rent a cricket or an ant

Cricket suicide via *Paragordius tricuspidatus*

- *Paragordius tricuspidatus* worm is known for manipulating the behavior of its host, the cricket *Nemobius sylvestris*.
- In its larval stage, the worm is microscopic, but grows into a large worm (4-6 in) inside its host since their eggs are laid at the edge of the water by rivers where crickets frequently reside.
- Upon ingestion, the worm (1 to 30) nourishes upon its host and fills the entire body cavity of the cricket, until maturation, when the parasitic worm is ready to exit into water to complete its life cycle.

- Also in grasshoppers, and ants

Light seeking crickets

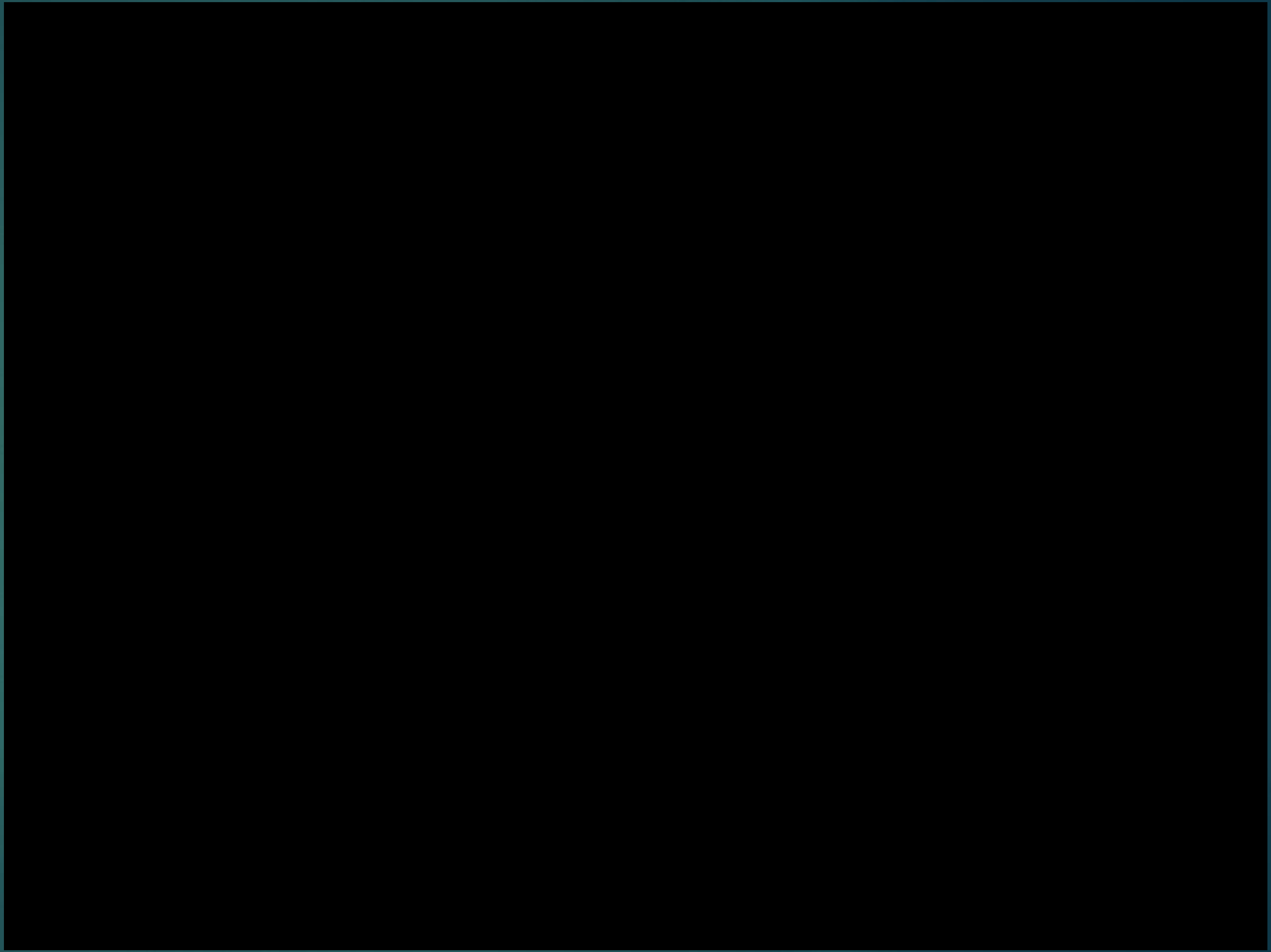
- The worm induces a peculiar light seeking behavior in its cricket host, leading them to open spaces and ponds (the surface of which reflects moonlight).
- Suicidally leap into water whereby the parasitic worm can slither out and find its mate, while the cricket often perishes.
- While crickets often drown in the process, those who survive exhibit a partial recovery and return to normal activities in as little as 20 hours
- Mermithidae nematode worms control arthropods. Get them to seek water by increasing amount of salt in their systems.

Nematode releases hormones which make cricket more attracted to light. Once cricket reaches light reflecting water, it jumps in and drowns and the worm (or up to 30 worms) emerges to find a mate.

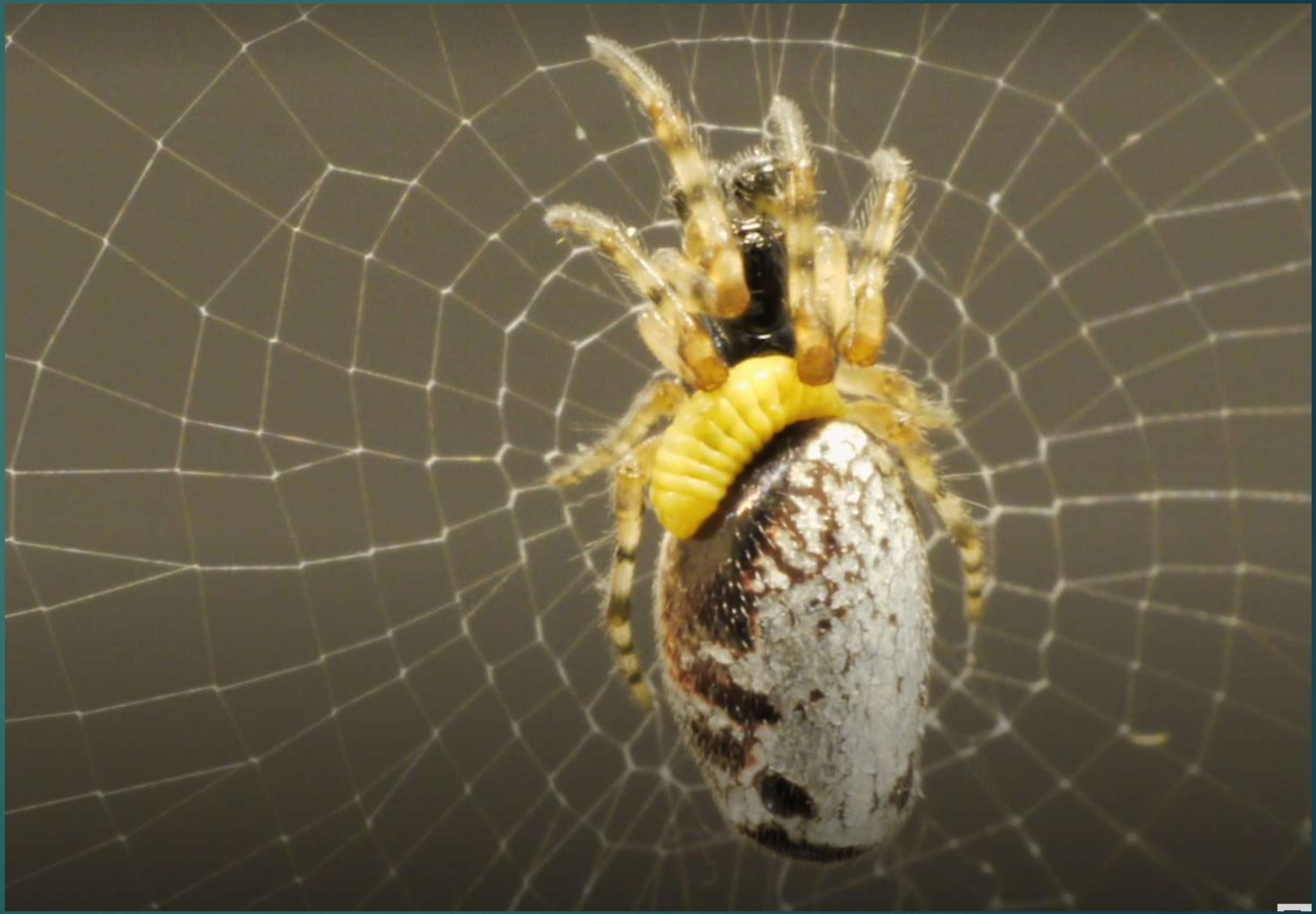
Horsehair worm

A nematomorph parasitoid worm emerges from the body of its grasshopper host

Wasp digs a hole



Spider parasites



Spiders made to reweave webs to protect wasp cocoon.

- The parasitic wasp *Hymenoepimecis argyraphaga* glues its egg on spiders of the species *Leucauge argyra*. After the larva emerges, it pokes a few holes in the spider's abdomen and sucks its blood.

- Shortly before killing its host the larva injects it with a chemical that changes its weaving behavior. Spider rips down its own web and builds a new one of a radically different shape. Instead of a multistranded net designed for catching flying insects, the new web is merely a few thick cables converging at a central point The larva then kills the spider and enters the cocoon to pupate. Having sucked its host dry, the larva spins its cocoon on a thread hanging from the intersection of the cables. Suspended in the air, the cocoon is nearly impossible for would-be predators to reach.

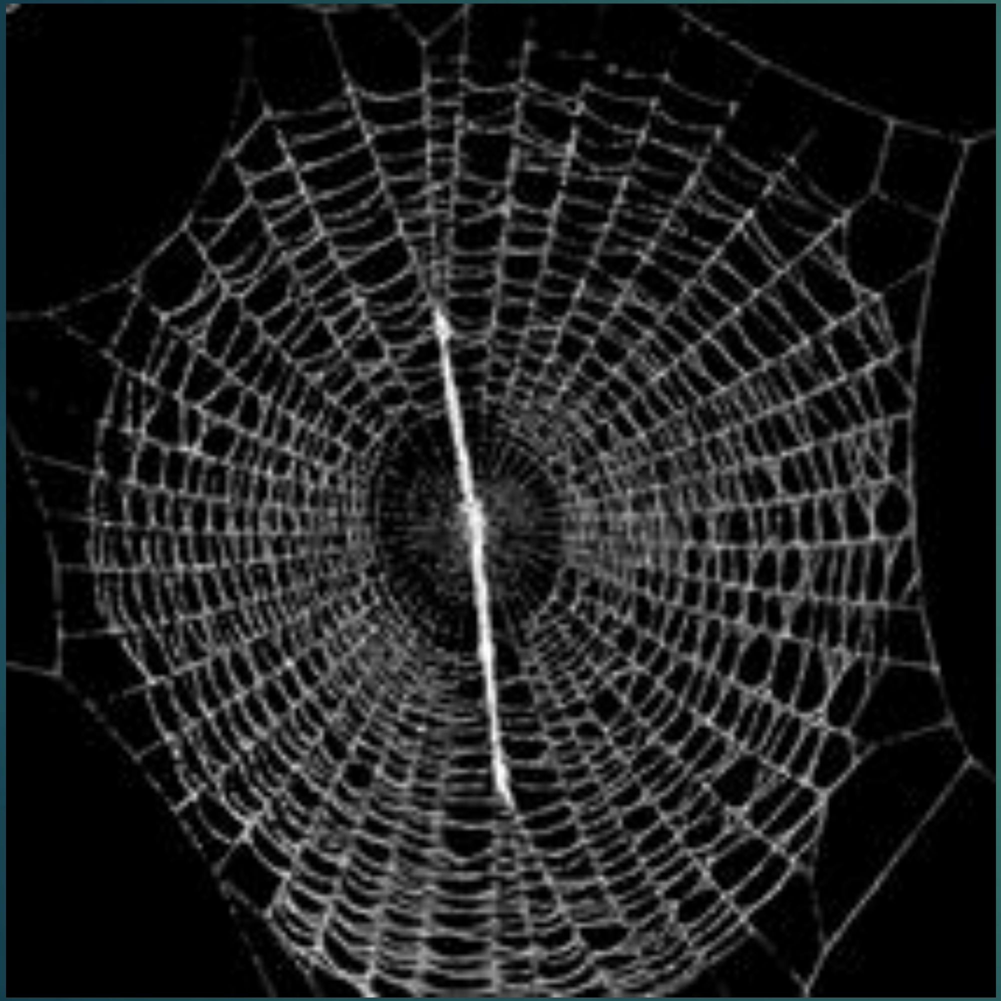
- Another example: Parasitic wasp larvae *Reclinervellus nielseni* attach to the spider *Cyclosa argenteoalba* and modify their web-building behavior in the same way. This manipulated behavior was longer lasting and more prominent the longer the larvae were attached to the spiders.

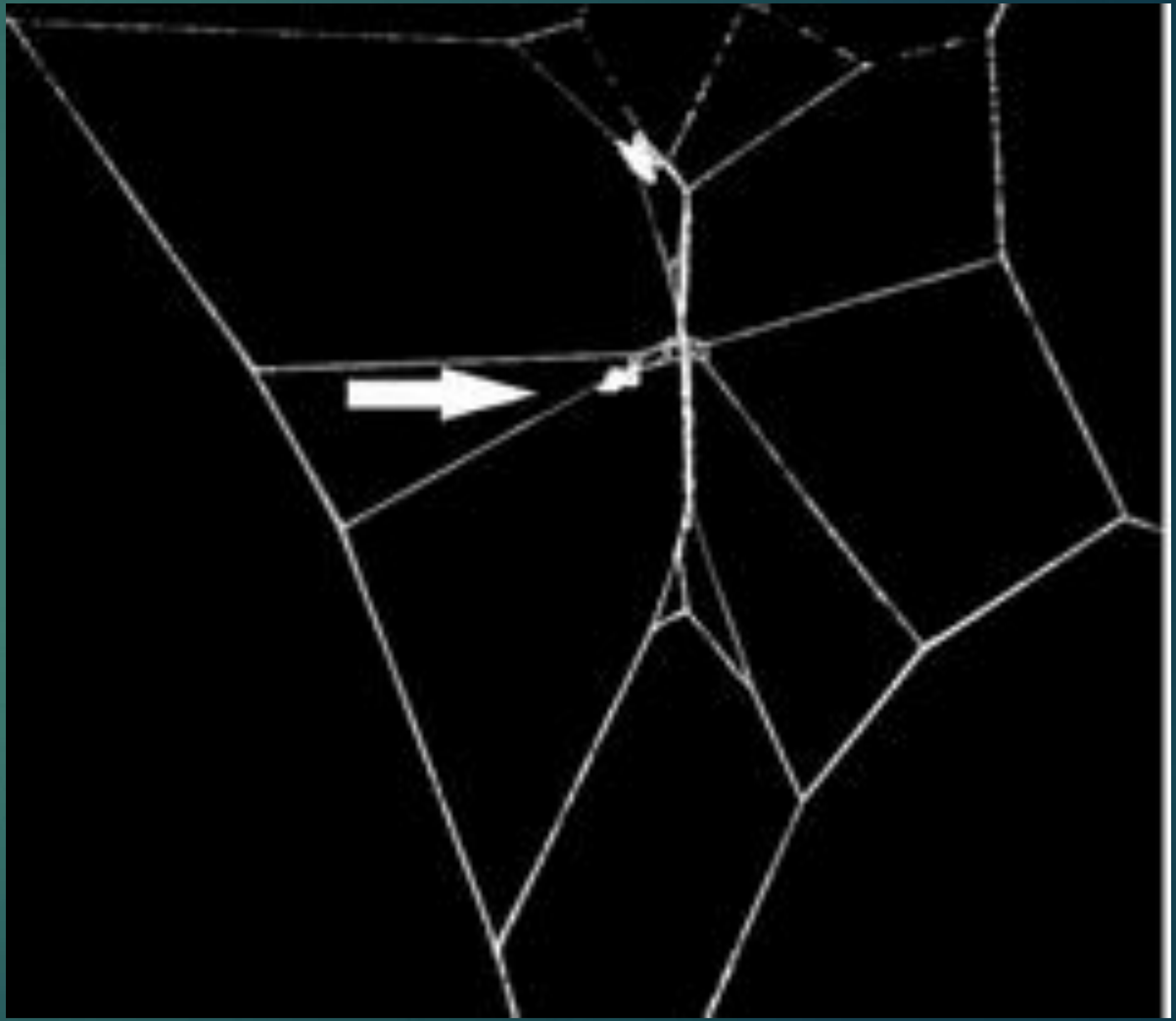
Web lover: Parasitic wasp Hymenoepimecis argyraphaga

Hymenoepimecis argyraphaga

Leucauge argyra spider

Web design reconfiguration via parasite control





Lays egg on spider’s back and makes it build special web

Web holds egg sa… d & eaten

Ophiocordyceps: Zombie making fungus

- The life cycle of Ophiocordyceps is like something from a sci-fi movie.
- Ants zombified by a fungus.
- Here’s how it works: Sometimes an ant, marching about its business outdoors, will step on a fungal spore. It sticks to the ant’s body and slips a fungal cell inside.
- The fungus, called Ophiocordyceps, feeds on the ant from within and multiplies into new cells. But you wouldn’t know it, because the ant goes on with its life, foraging for food to bring back to the nest. All the while, the fungus keeps growing until it makes up nearly 50% of the ant’s body mass.

Ophiocordyceps: Zombie making fungus: Ant fungus infection

Ophiocordyceps: Zombie making fungus

- But ants are good at disposing of sick ants, so fungus must keep infected ant looking normal for about 3 weeks. The fungal cells then send chemical signals to the ant’s brain, causing the host to do something strange.
- Produce chemicals that alter the navigational sense of their ant hosts. The ant departs its nest and climbs a nearby plant.
- the fungus drives ants upward, to a leaf above the ground. The ant bites down, its jaws locking as it dies.
- The fungus sends out sticky threads that glue the corpse to the leaf. And now it is ready to take the next step in its life cycle: Out of the ant’s head bursts a giant stalk, which showers spores onto the ant trails below.
- ’While the manipulated individual may look like an ant, it represents a fungal genome expressing fungal behavior through the body of an ant’. David Hughes (Penn State Univ)

Cordyceps fungus: alters ant navigational ability

- A carpenter ant falling victim to parasitic fungus of the genus *Cordyceps* is manipulated to produce a behavior that facilitate dispersal of the fungus.
- Produce chemicals that alter the navigational sense of their ant hosts.
- Fungus attaches spores to the cuticle of the ant. The spores then germinate and break into the ant's body and grow there.
- The fungus then produces chemicals that cause the ant to climb to the top of a tree or plant and clamp its mandibles around a leaf or leaf stem to stay in place; never done by normal ants.
- When the fungus is ready to produce spores, it eventually feeds on the ant's brain and thus kills it.
- The fruiting bodies of the fungus then sprout out of the cuticle and release capsules filled with spores. The airborne capsules explode on their descent.

Hughes, 2015

Ophiocordyceps fungus & Amazonian ant Dinoponera longipes

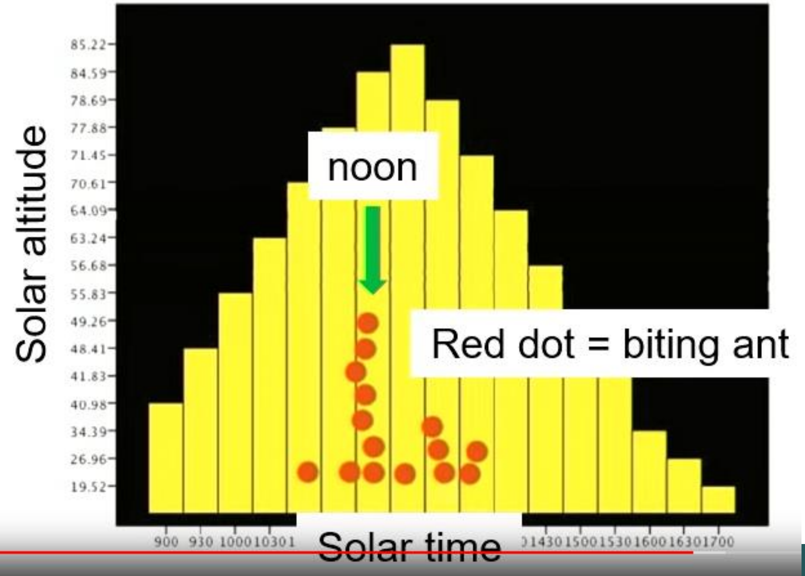
Gets ant to climb a plant, to end of a leaf where it kills ant and produces spore stalks.

Different fungi have different ant hosts that end up on different parts of tree above ant foraging lines.

Fungus spore sticks to exoskeleton and enzyme rots cuticle and explodes inward. Over 3 weeks reproduces. Ends up being 50% of ant weight.

Zombies at high noon

- ‘Normal ants’, high in canopy, late morning leave colony, turn into zombies, random walk,
- staggering like horror film ‘mummies’, repeated convulsions that make them fall down,
- ~25 cm from ground, walk to leaf, underside,



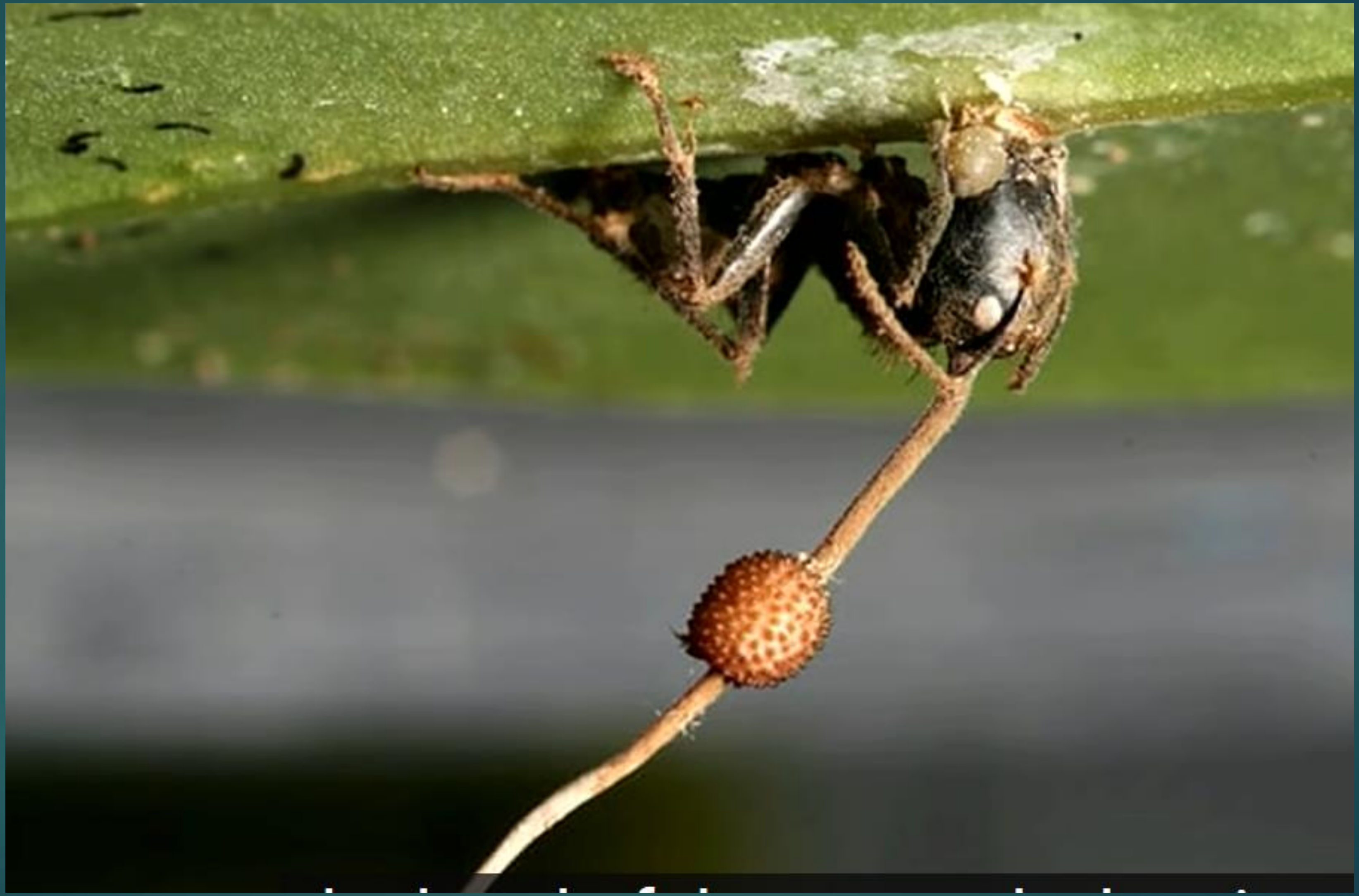
Hughes et al (2011) Behavioral mechanisms and morphological symptoms of zombie ants dying from fungal infection. *BMC Ecology* 11: 13.

Zombies at High Noon: Next, at exactly noon, it flees the colony and ends up on plant stalk exactly 10 inches off floor above ant trail. Always underside of leaf. Drives mandibles into leaf in death grip. And then it dies.

Ant dies and fungus begins growing

Stage 3: grows reproductive stalk

Fruiting body explodes, showering spores unto ant trails below



After This Fungus Turns Ants Into Zombies, Their Bodies Explode

Ophiocordyceps buquetii glowing from Polyrhachis, a species of ant in Ghana.

Ophiocordyceps humbertii after attacking a species of Brazilian Amazon wasps

Ophiocordyceps dipterigina on a fly in the Adolfo Ducke Forest Reserve in Brazil

Ail Ophiocordyceps species sprouting from a Pseudomynnex ant in the Brazilian Amazon.

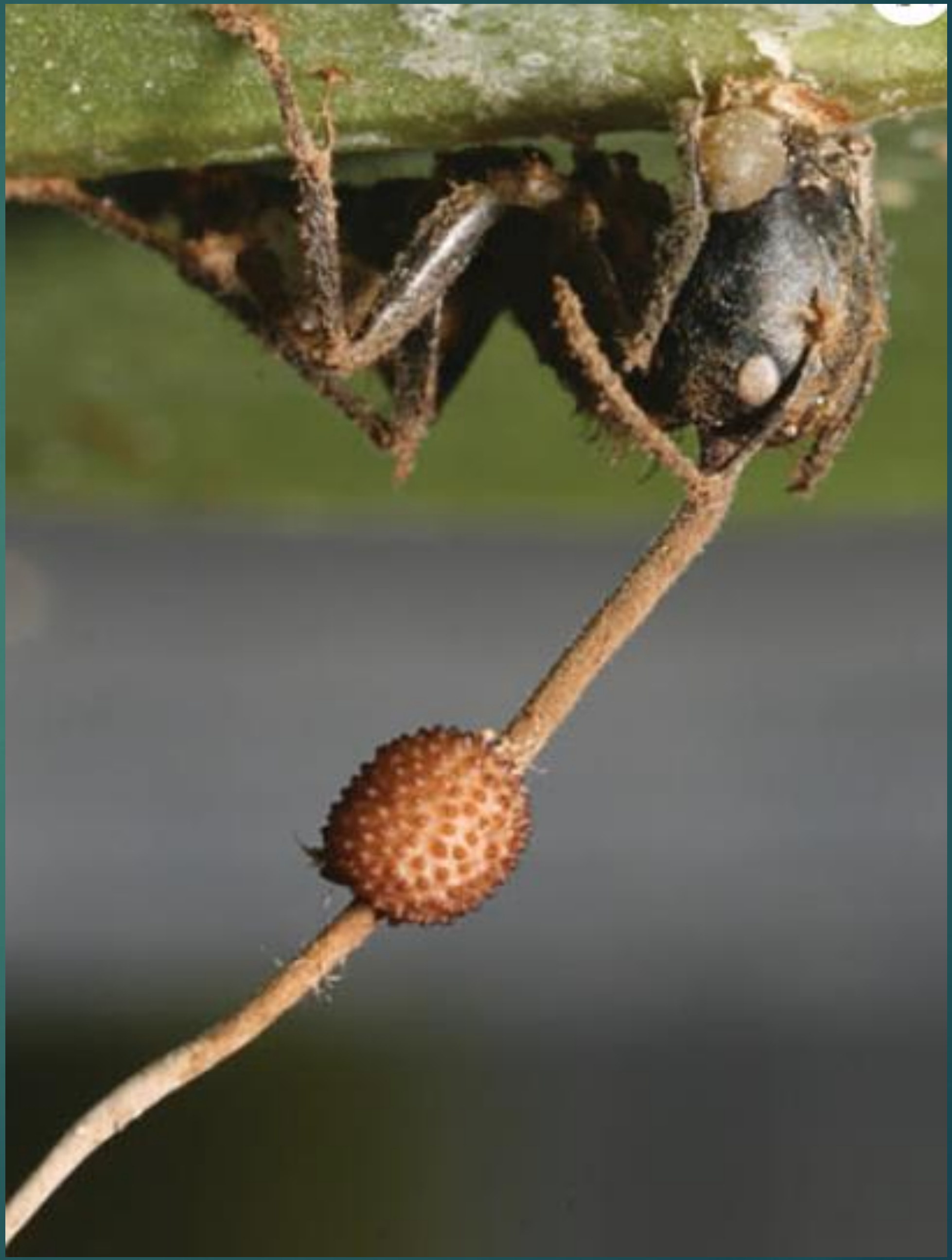
A cicada on the Amami Islands of Japan that fell prey to Ophiocordyceps longissima.

A sprout of Ophiocordyceps grows from the head of Camponotus atriceps, a species of carpenter ant, in the Brazilian Amazon

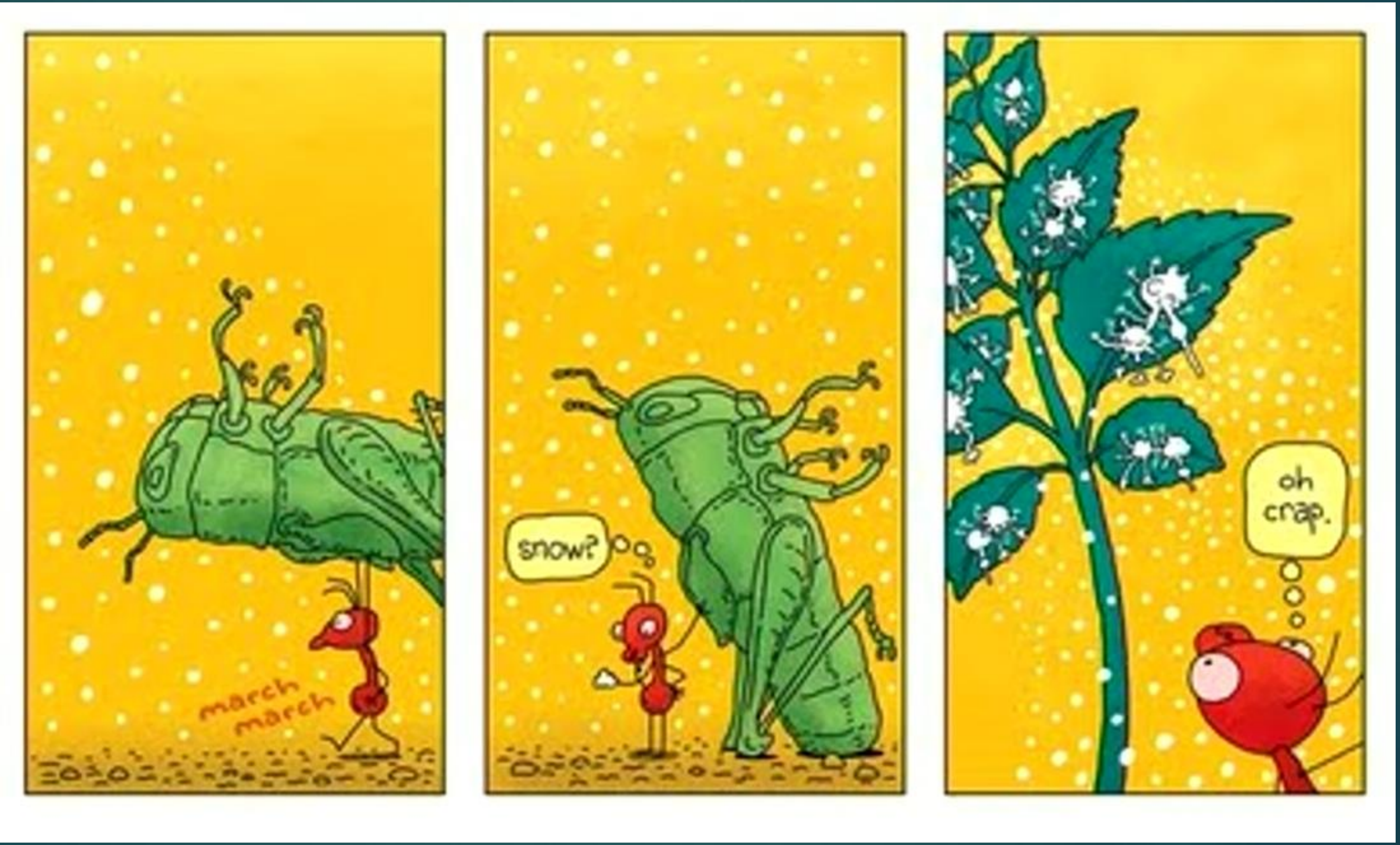
A species of Ophiocordyceps sprouts from Camponotus novogranadensis, an ant species, in Itacolomi State Park in Brazil

Ophiocordyceps camponoti-renggerii spreading from an ant in the Adolfo Ducke Forest Reserve in Brazil.

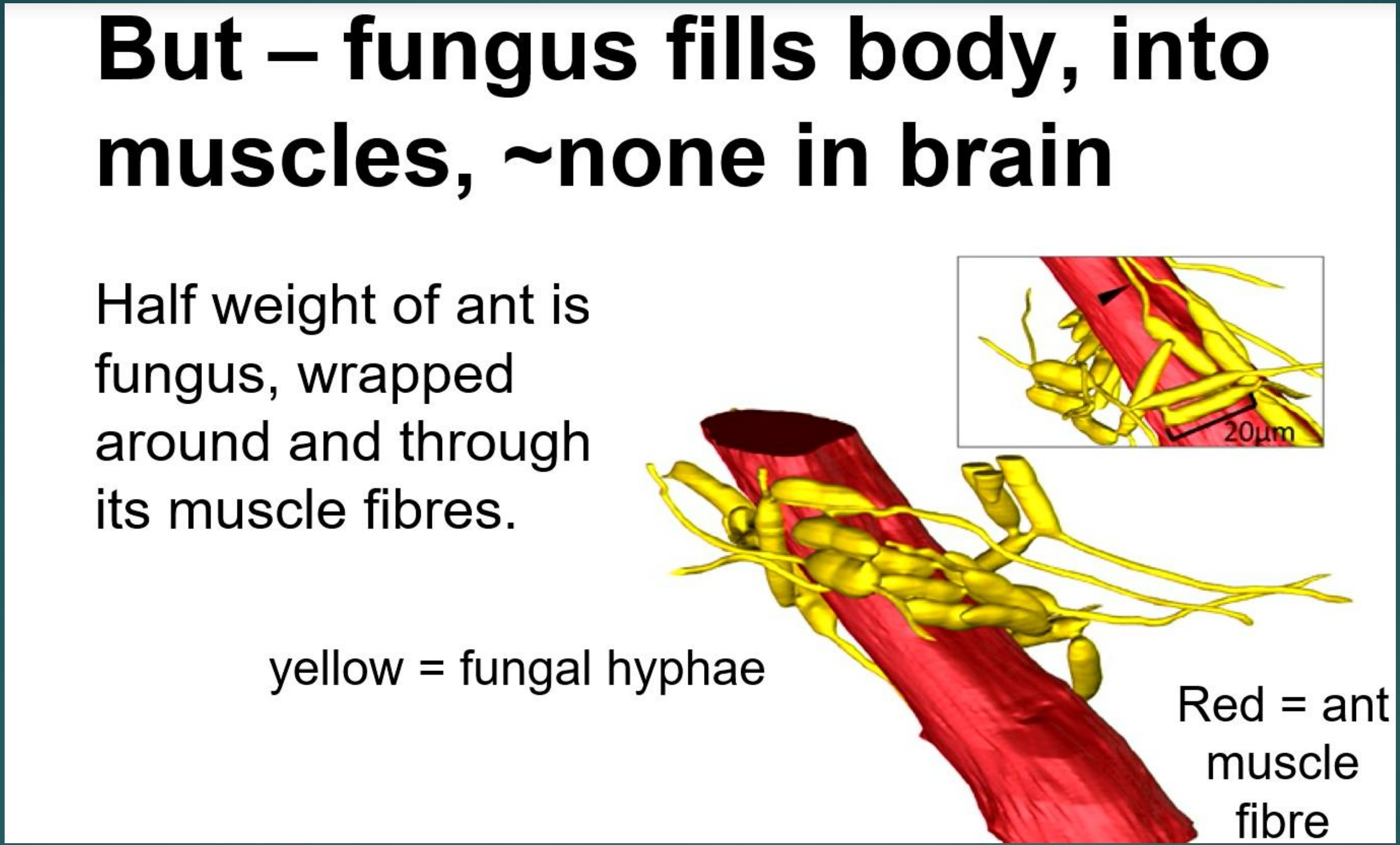
O. unilateralis stroma issuing from the head of a dead C. leonardi whose mandibles are attached to the lower surface of a major plant vein



Cartoon version



Not brain control?

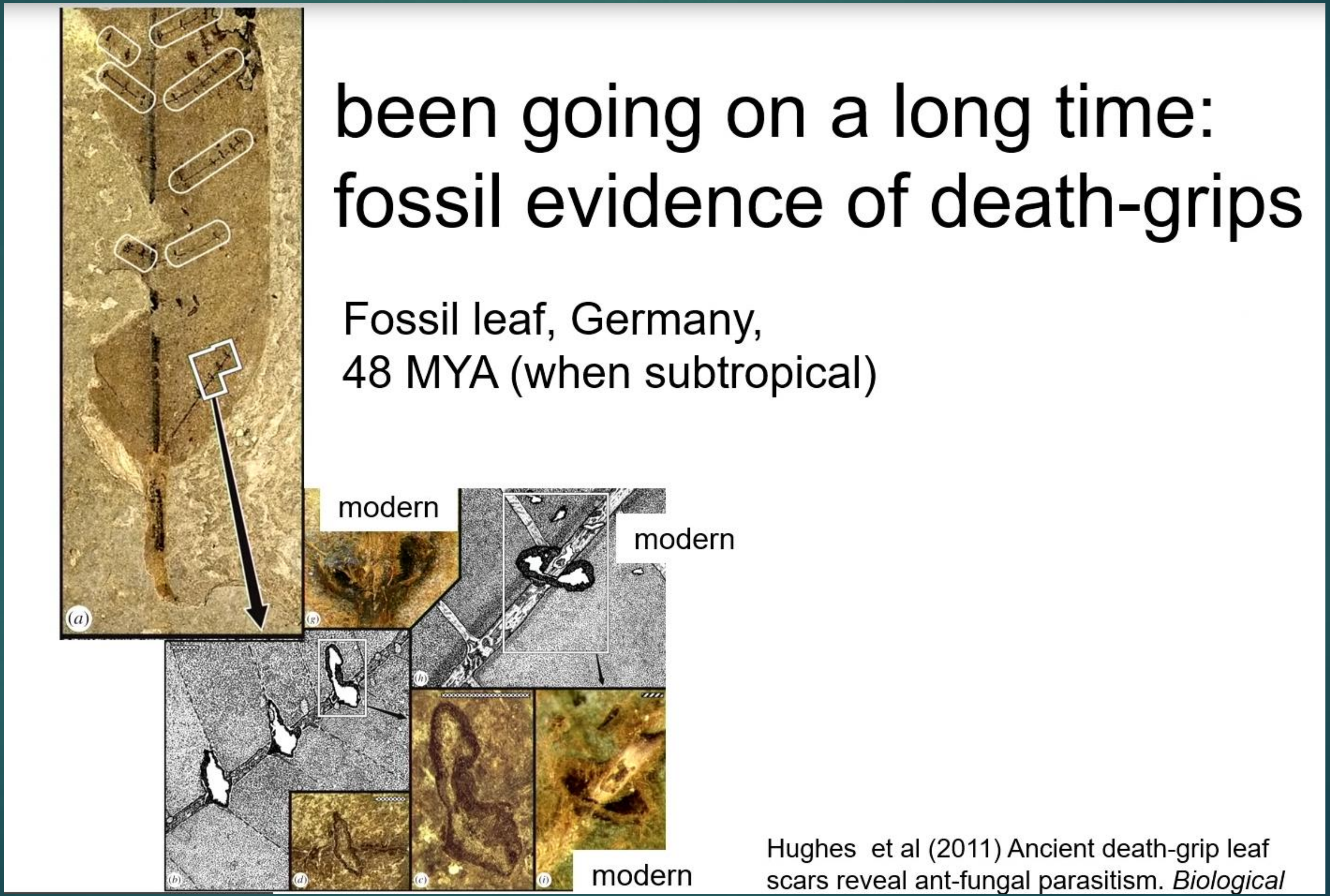


But fungus is related to ergot (origin of LSD)

600 Cordyceps fungus species: for each its own insect

More numerous an insect species becomes more likely it will be attached by cordyceps fungus

48 million years: evidence = exact same fossil bite mark



Drugged, Castrated, Eager to Mate: The Lives of Fungi-Infected Cicadas

When cicadas are infected by a parasitic fungus, the insect's innards get digested and their rear ends are replaced by a chalky white plug of spores. Kasson et al.

Massospora fungus: To transport its spores, it uses the cicada's living body, which spreads the fungus as it mates, like an STD. Laced with amphetamine and psilocybin; act as appetite suppressants

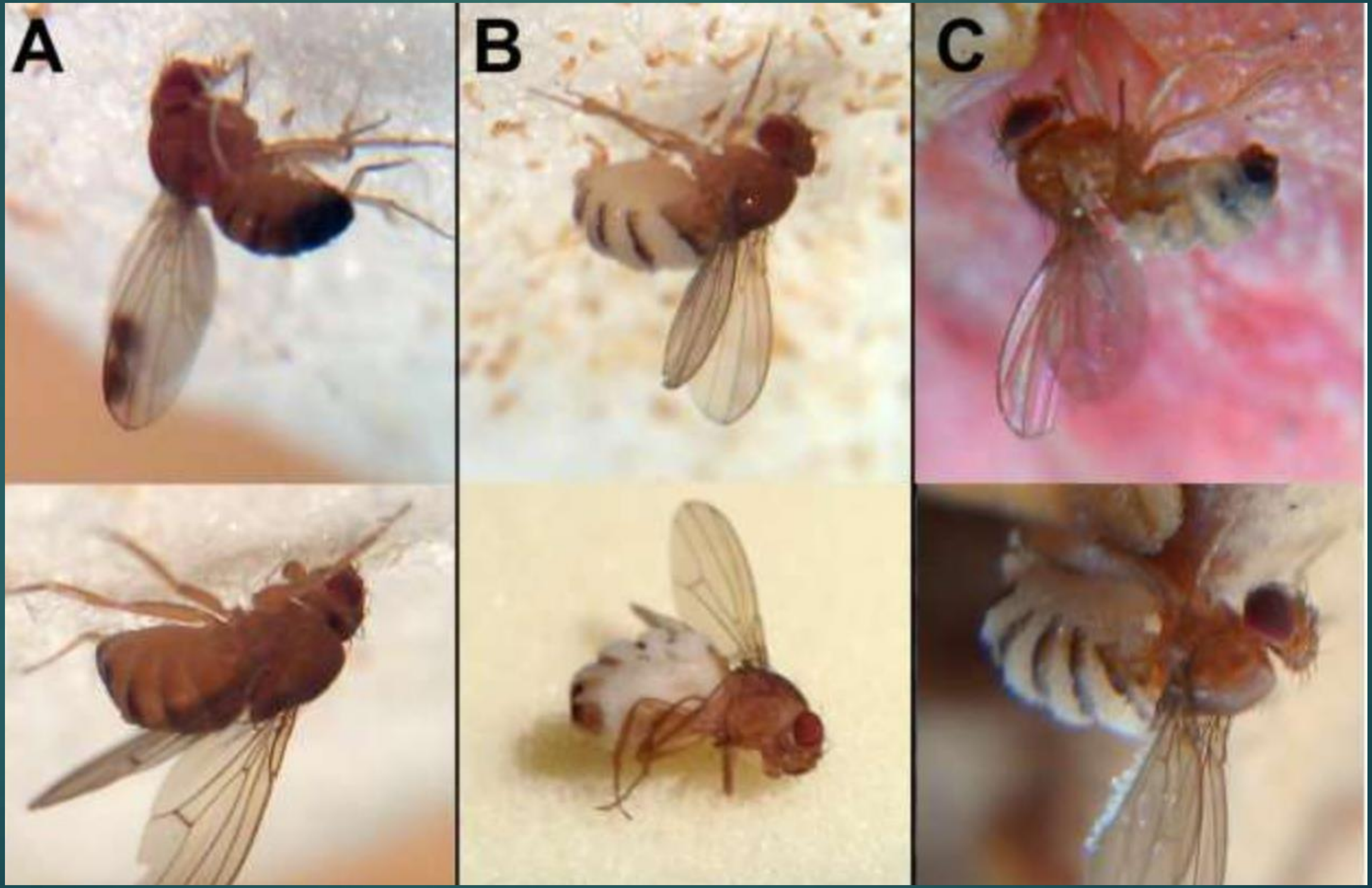
Zombie flies: Entomophthora muscae

- After Entomophthora muscae fatally infects house flies, it makes microscopic stalks for hurtling spores at other insects that come nearby.
- The fungal cells release cuticle-cutting enzymes and slip inside the insect's body. There, the fungus grows into long threadlike structures, digesting the fly's guts and penetrating its brain until the poor insect finally dies.
- But E. muscae determines when and where the fly dies so that it is in the best position to release fungal spores onto other unsuspecting flies. By exerting a bit of mind control, the fungus forces the fly to seek an elevated perch and lift its wings in an unnatural position. This allows the fungus to grow from the insect's back and abdomen, taking the form of stripes of white fuzz, even after the fly dies.

Fruit fly fungus: glues itself to summit area, wings out, dies and spores flood out for hours

Entomophthora muscae, which means “fly destroyer.” It lives off houseflies and fruit flies, among others.. “The fungus only kills at dusk.” On 4^{th} or 5^{th} day of infection

Death with wings up: fungal infection



Hyperparasite – another fungus

A hyper fungus infects prior fungus
and stops its spore production

A hyperparasitic fungus — a parasite of a parasite — on an Ophiocordyceps species, which itself infected a Camponotus ant in Japan.

Hyper fungus that "castrates" the zombie-ant fungus.

Another fungus keeps the zombie-ant fungus in check.

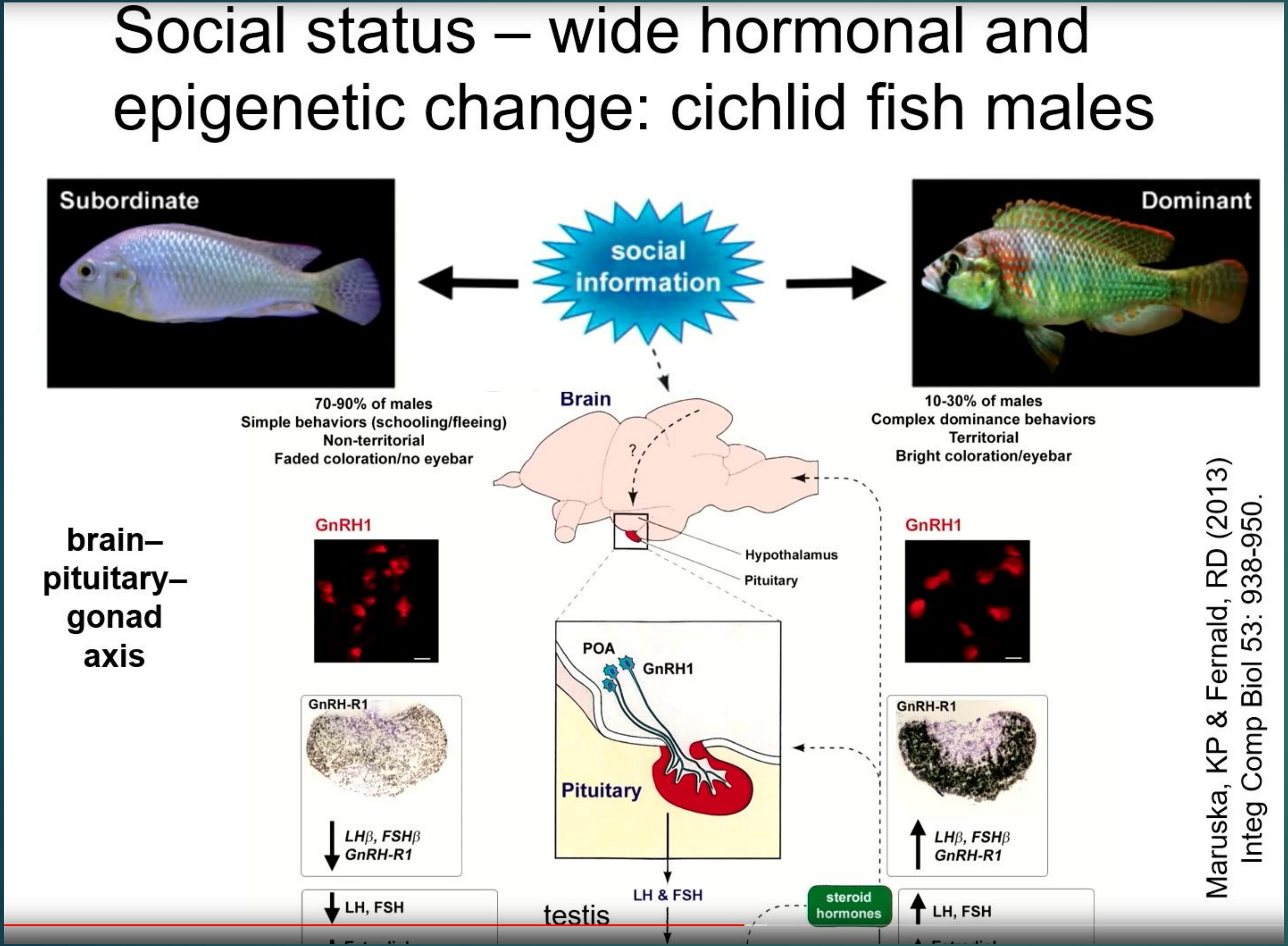
The fungus-killing fungus chemically "castrates" its zombie-making cousin

Only 7 percent of zombie-ant fungus specimens were able to produce spores—meaning that the unnamed fungus largely limits *Ophiocordyceps'* spread.

Money making *Ophiocordyceps sinensis*: Caterpillar fungus in Tibet harvested: 1500 = $100 K: cream protects their faces from high-altitude windburn.

“Caterpillar fungus" - which infects the caterpillars of ghost moths.

- The host of *O. sinensis* are ghost moth caterpillars, which live underground munching on the roots of plants. So unlike the ant-infecting zombie fungi that can simply scatter their spores around areas where their ant hosts are likely to walk by, such means of dispersal would be ineffective for reaching caterpillars that spend their entire time underground
- Roots of *O. sinensis*' fame is based on the fungus' prized medicinal properties, which has been known and documented for centuries in China where it is known as *dōng chóng xià cǎo* (冬蟲夏草: which translates into "winter worm, summer grass).



Radical changes when a subordinate becomes dominant via hormonal and epigenetic changes

It may be that parasites may gain control via manipulation of these epigenetic systems

Mimicry of old age: Microsporidia (*Nosema ceranae*)

- A unicellular parasite, Microsporidia (*Nosema ceranae*), infects honey bees (*Apis mellifera*) and affects a range of individual and social behaviors in young adult bees.
- In social bees, many special functions are based on age.
- The infection of bees causes them to exhibit behaviors typical of older bees.
- Infected bees also have significantly increased walking rates and higher rates of food exchange.

Lecocq et al., 2016.

Drosophila Defenses

- Most known parasitoid wasp species attack the larval or pupal stages of Drosophila.
- While Trichopria drosophilae infect the pupal stages of the host, females of the genus Leptopilina and Ganaspis attack the larval stages.
- A biological arms race: Parasitic wasps have tremendous value as biocontrol agents.

Booze: fruit fly protector

- Some fruit flies, however, can overcome the effects of wasp venom and mount an immune response against wasp eggs.
- The blood cells in these fly larvae swarm over the wasp eggs and release nasty chemicals to kill them, allowing the fruit fly larvae to grow into adults.
- Infected fruit flies that consumed alcohol beat out the wasp eggs in about 60 percent of the cases, compared to a 0 percent survival rate for fruit fly controls that fed on plain yeast.
- A developing wasp knocked out within an alcohol-consuming fly larva dies in a particularly horrible way. "The wasp's internal organs disperse and appear to be ejected out of its anus. It's an unusual phenotype that we haven't seen in our wasps before
- The lab repeated the experiment using another species of wasp that specializes in laying its eggs in *D. melanogaster*, rather than the generalist wasp used previously. Again, 80 percent of the infected flies wound up on the alcohol side of the dish, while only 30 percent of the uninfected flies did. But the alcohol diet was far less effective against the specialist wasps, killing them in only 10 percent of the cases.

Booze and fruit flies

- Alcoholic drinks aren’t generally put into the category of health food, but in some cases they might be just the cure for nasty parasites.
- The fruit fly larvae eat the rot, or fungi and bacteria, that grows on overripe, fermenting fruit. They're essentially living in booze.
- The amount of alcohol in their natural habitat can range from 5 to 15 percent. Imagine if everything that you ate and drank all day long was 5-percent alcohol. Fruit flies are really good at detoxifying alcohol.
- Tiny, endoparasitoid wasps are major killers of fruit flies. The wasps inject their eggs inside the fruit fly larvae, along with venom that aims to suppress their hosts' immune response. If the venom is effective enough, the wasp egg hatches, and the wasp larva begins to eat the fruit fly larva from the inside out. Eventually, an adult wasp emerges from the remains of the fruit fly pupa.

A dissected fruit fly infected by the Howardula parasite, but not by protective Spiroplasma. The mother parasite is at bottom right, and larvae around the fly./John Jaenike.

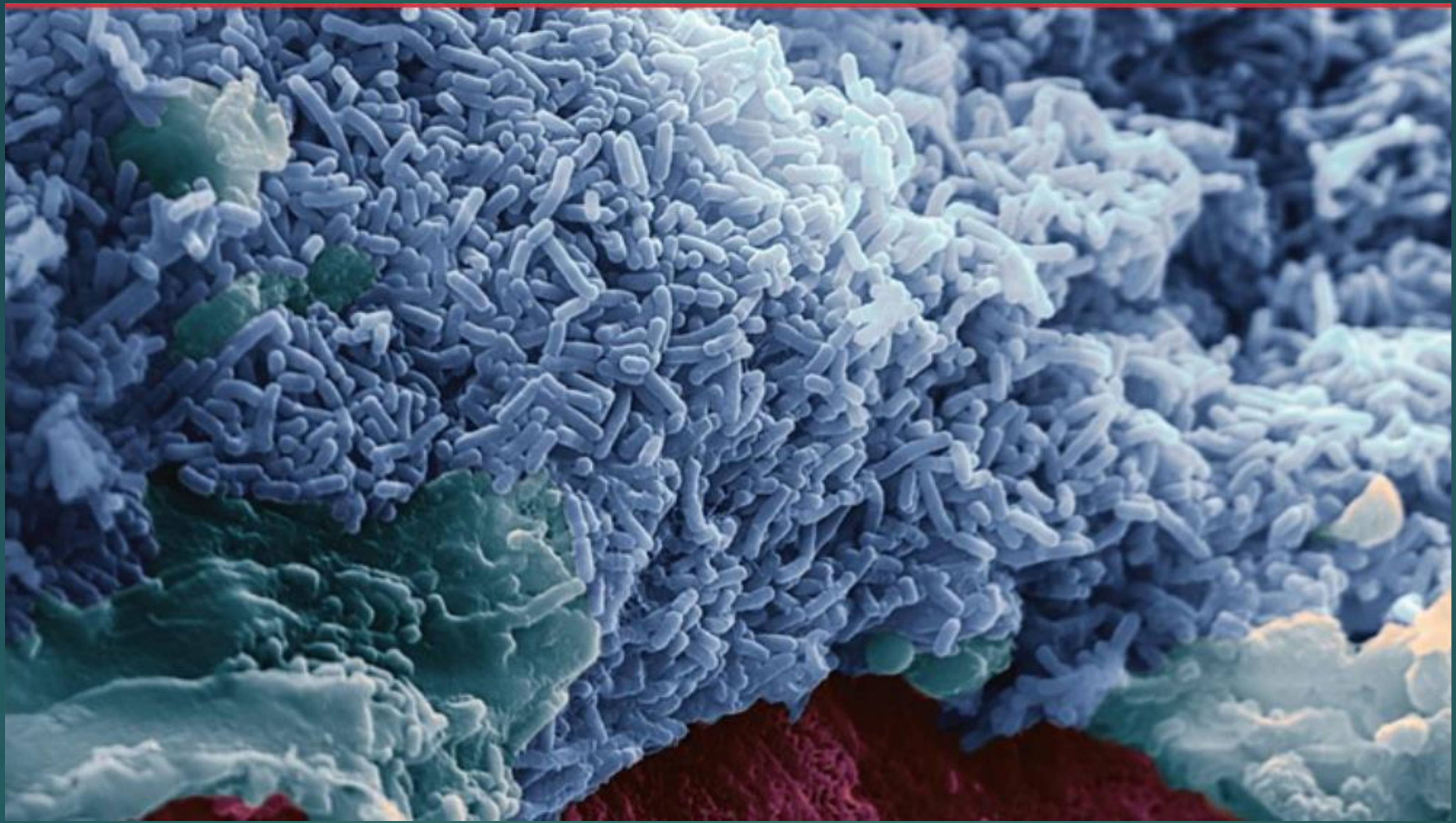
Drosophila neotestacea fly

- Nightmarish infections of the *Drosophila neotestacea* fly species by *Howardula aoronymphium*, a roundworm parasite.
- A mother *Howardula* worm would swell to massive size inside a host fly, laying thousands of eggs. After they hatched, larvae coursed through the host's body. The flies didn't die, but they no longer had the strength to reproduce. The worms infest nearly one in four *D. neotestacea* flies, and sterilization seemed absolute.
- But in some flies, *Howardula* didn't lead to sterilization. Instead it was the worms who were sickly, and their offspring few. And the only difference between fertile and infertile *Howardula*-infected flies was the presence of a bacteria called *Spiroplasma*.

Spiroplasma

- *Spiroplasma* is racing through fruit flies across North America. In the early 1980s, it was present in just 10 percent of eastern fruit flies. Now it's in 80 percent, and moving rapidly west.
- The pattern fits with what's predicted by traditional evolutionary theory: A beneficial mutation arises, confers a reproductive advantage, and over time spreads through a population -- except that the adaptation isn't genetic, but bacterial. Microbes can be passed from mother flies to offspring, but also carried by mites between flies, and even between species.
- It's essentially an alternative immune system.
- Other examples of insect endosymbioses include Moran's specialty, a microbe that protects aphids from parasitic wasps.
- Another bacteria called *Wolbachia* causes some male insects to turn female -- a relationship that doesn't make obvious evolutionary sense. In one species of fruit fly, *Wolbachia* can also kill all male offspring, but only if their mother alone is infected. If both parents are infected, the offspring are fine.

Lactobacillus promotes social interaction in mice



Scientists determined that *Lactobacillus reuteri*, (colorized and shown here) stuck to gut tissue, somehow promotes social interaction in mice. If born without it, less social. If reintroduced, more social. Sends signals to brain via vagus nerve which signals for more oxytocin.

Microbiome: Feeling it in your gut

- The **human microbiome** is the aggregate of all microbiota that reside on or within human tissues and biofluids along with the corresponding anatomical sites in which they reside, including the skin, mammary glands, placenta, seminal fluid, uterus, ovarian follicles, lung, saliva, oral mucosa, conjunctiva, biliary tract, and gastrointestinal tract. Types of human microbiota include bacteria, archaea, fungi, protists and viruses.
- Humans are colonized by many microorganisms; the traditional estimate is that the average human body is inhabited by ten times as many non-human cells as human cells, but more recent studies estimate that ratio as 3:1 (37 trillion human cells) or even 1:1.
- 2,000,000 bacterial genes to 20,000 human genes in human body
- 200 million neurons in human gut; vagus nerve is like a superhighway between the gut and the brain; most serotonin produced in gut

Microbiome and Brain

- Intestinal microbiota are linked to mood, behavior, and cognition.
- Current theories: anxiety, stress response, depression, Parkinsonism. obesity, diabetes, autism are gut connected
- Therapeutics: neurologists have known that putting children with epilepsy on a specific diet can reduce their seizures. This so-called ketogenic diet is low in carbohydrates and high in protein and fat. May increase GABA. In the brain, GABA acts like a sort of brake for brain cells, reducing the activity of neurons
- Two bacterial genera, *Coprococcus* and *Dialister*, were consistently depleted in individuals with depression.
- Correlational mouse studies

Bibliography

- Popular science books

  - *Simon, M (2018) Plight of the Living Dead: What real-life zombies reveal about our world— and ourselves.*
  - *Simon, M (2016) The Wasp that Brainwashed the Caterpillar*
  - *Wyatt, TD (2017) Animal behaviour: A very short introduction. OUP*
  - *Zimmer, C (2003) Parasite Rex: Inside the bizarre world of nature's most dangerous creatures. Arrow.*
  - *Zuk, M (2008) Riddled with Life: Friendly worms, ladybug sex, and the parasites that make us who we are.*

- Science journalism on the web:

  - Ed Yong e.g. (2017) How the zombie fungus takes over.../
  - Carl Zimmer (2014) Mind suckers.

Bibliography

- Mind Control: How Parasites Manipulate Cognitive Functions in Their Insect Hosts - Frederic Libersat, et al., 2018
- Books and special collections of papers
  - Special issue of *Integrative and Comparative Biology*, Vol 54, Issue 2. Parasitic manipulation of host phenotype, or how to make a zombie. Free, available at www. academic, oup.com/icb/issue/54/2
  - Dawkins, R (1982) *The extended phenotype.*.
  - Hughes, DP, Brodeur, J & Thomas, F (eds.) (2012) *Host manipulation by parasites.*

Contact Info

- Charles J. Vella, PhD
- www.charlesjvellaphd.com
- charlesvella@comcast.net
- 415-939-6175