Honey bee viruses

The good, the bad and the ugly

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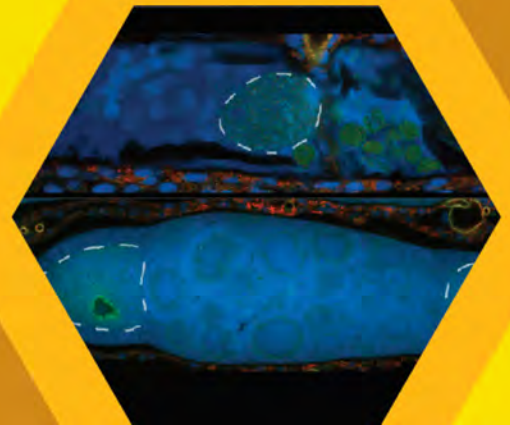
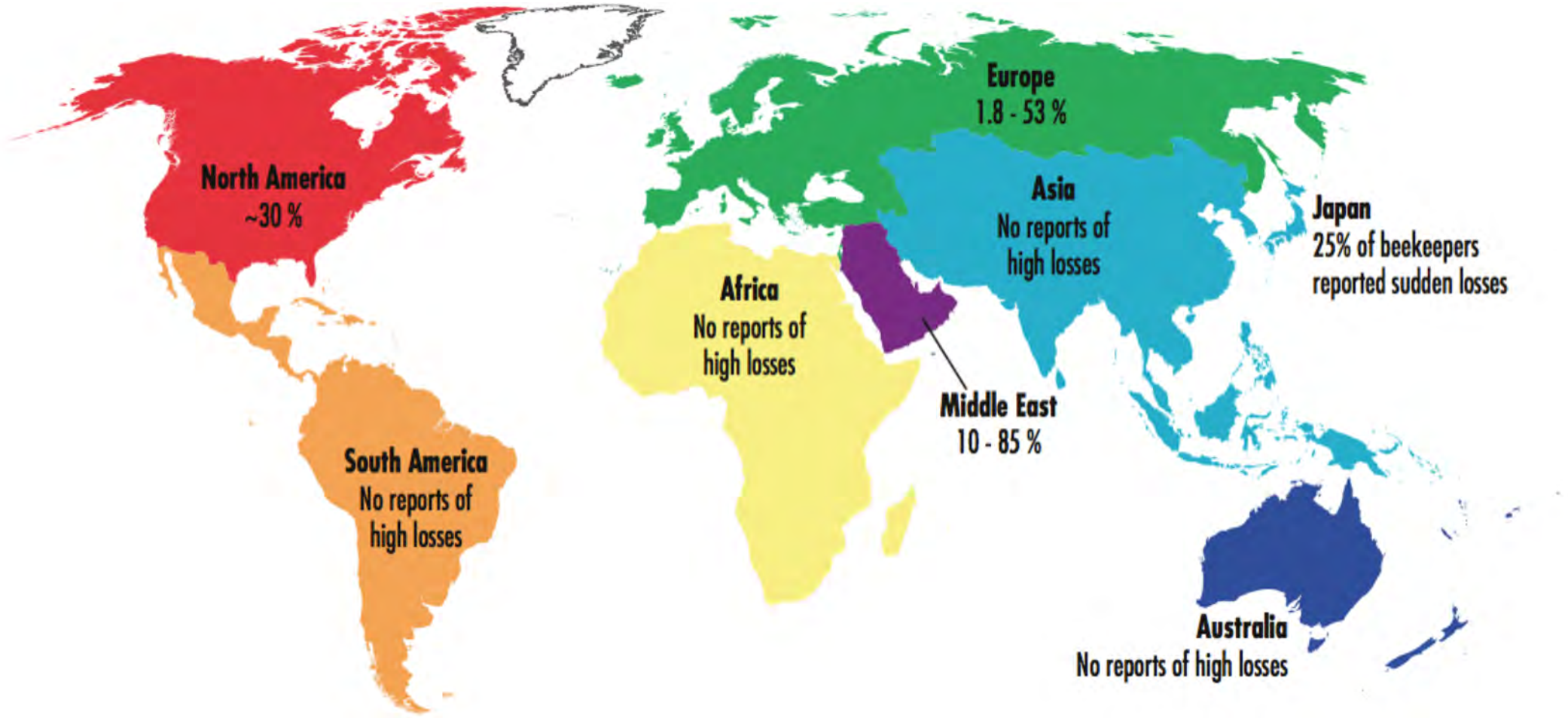
http://sydney.edu.au/science/biology/socialinsects/

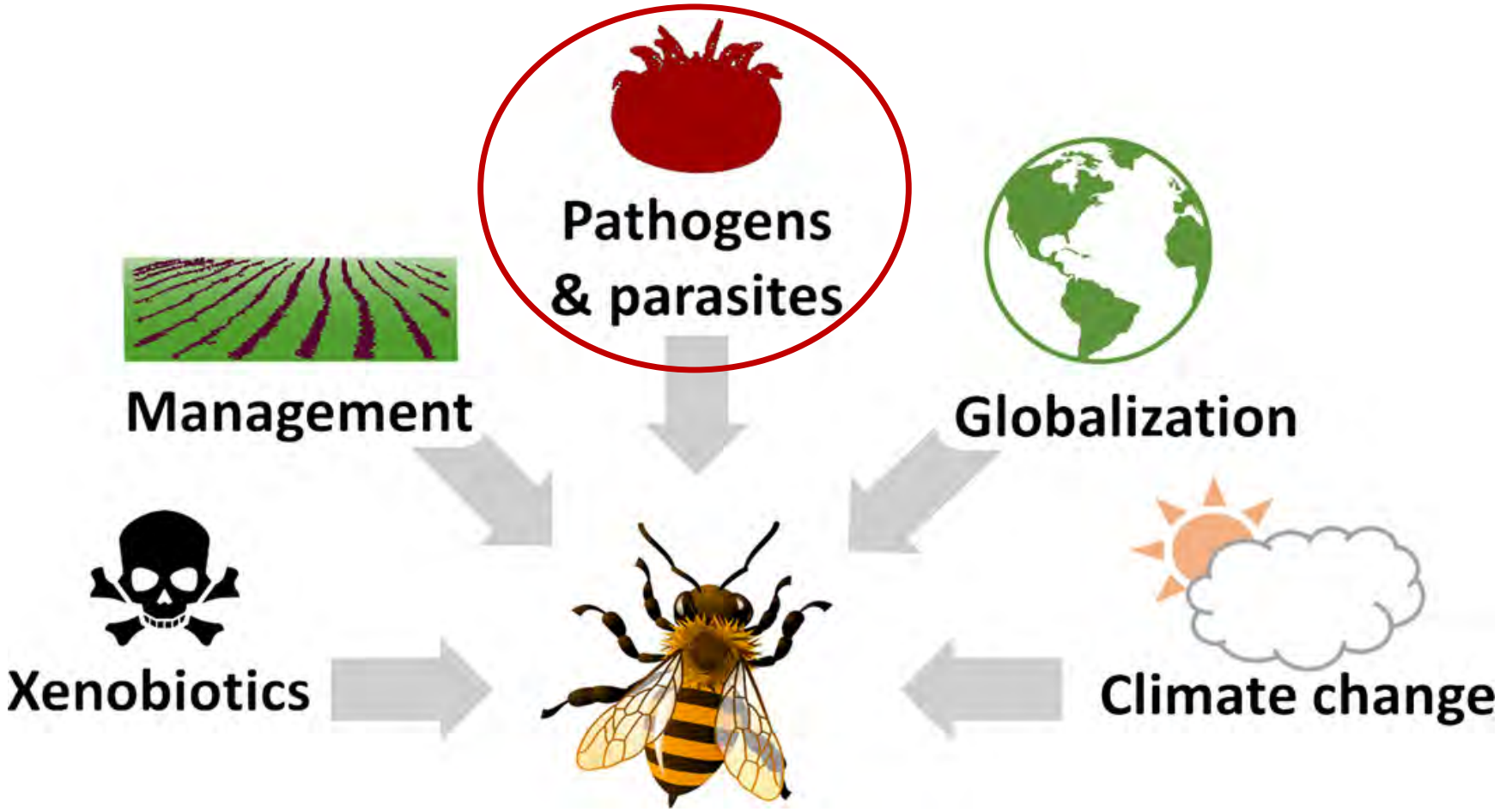
https://www.facebook.com/sydneybeelab/



Honey bees in decline



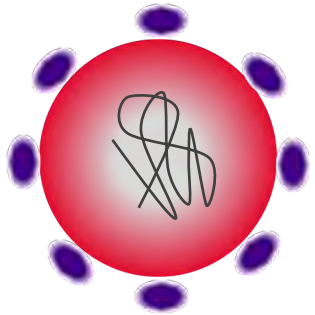
Factors affecting honey bee health



Trapp, J., et al **2017** *Genomics, transcriptomics and proteomics: enabling insights into social evolution and disease challenges for managed and wild bees.* Mol Ecol **26**(3): 718-739.

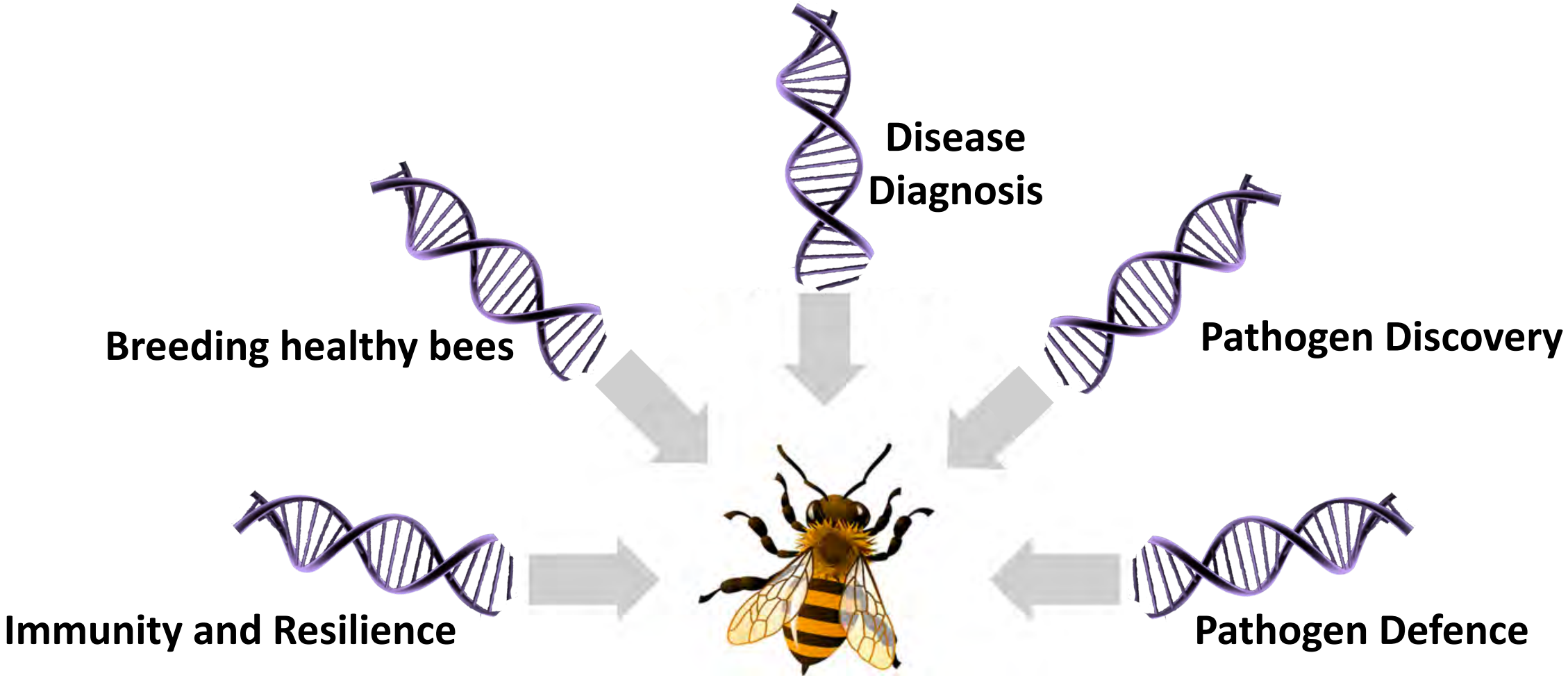
What can we do about bee disease?

Parasites and pathogens are a major cause of colony loss and suboptimal honey bee health



Are there genetic mechanisms that could reduce the impact of viruses in honey bees?

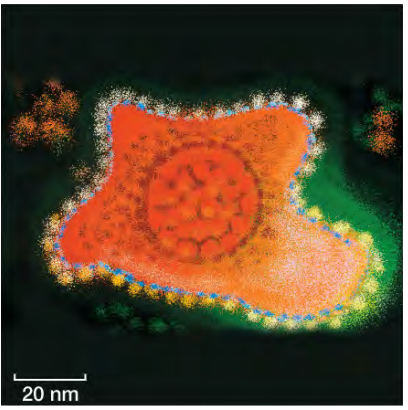
The power and promise of genomics for honey bee health

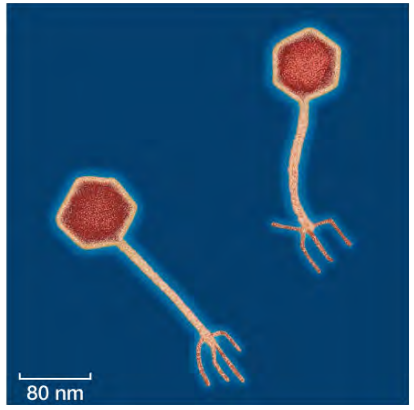


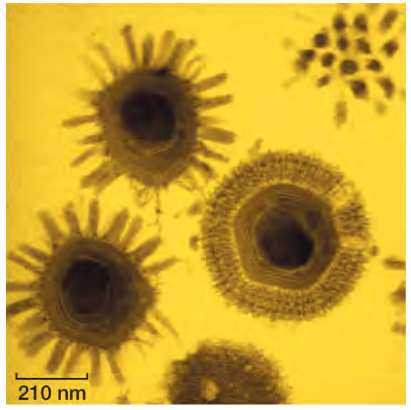
Grozinger, C. M. and G. E. Robinson (2015). "*The power and promise of applying genomics to honey bee health.*" Curr Opin Insect Sci **10**: 124-132.

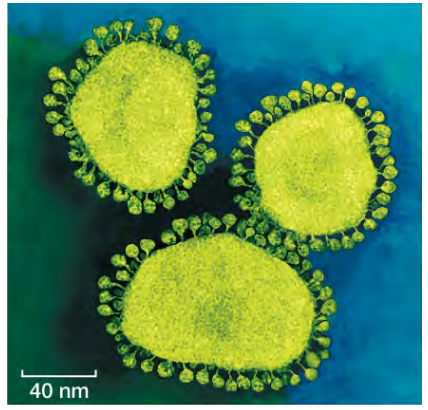
My goals

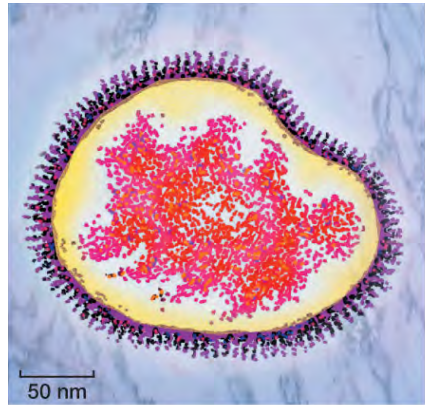
1. Understand the impact of new pests and diseases on honey bees
2. Investigate methods to improve honey bee health

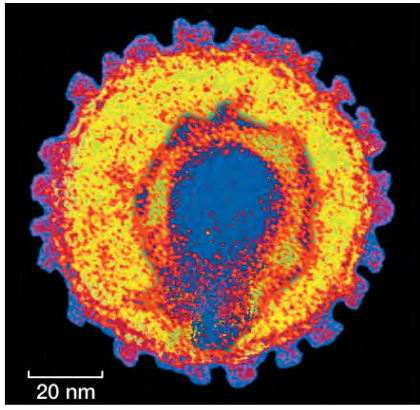












Viruses

Infect all cellular forms of life

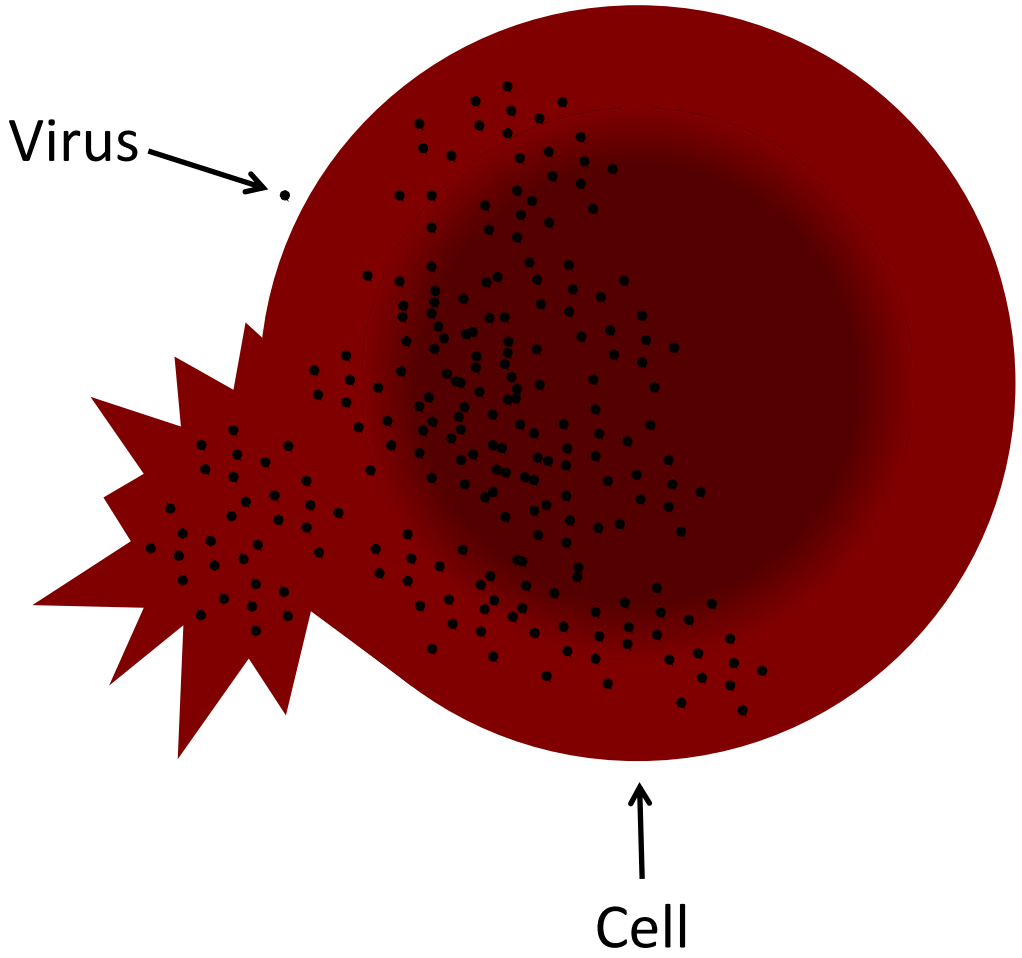
Abundant

Diverse

Rapidly evolving

http://www.macmillanhighered.com/BrainHoney/Resource/6716/digital_first_content/trunk/test/hillis2e/hillis2e_ch19_5.html

Viruses



Virus genomes come in different flavours

GENOME

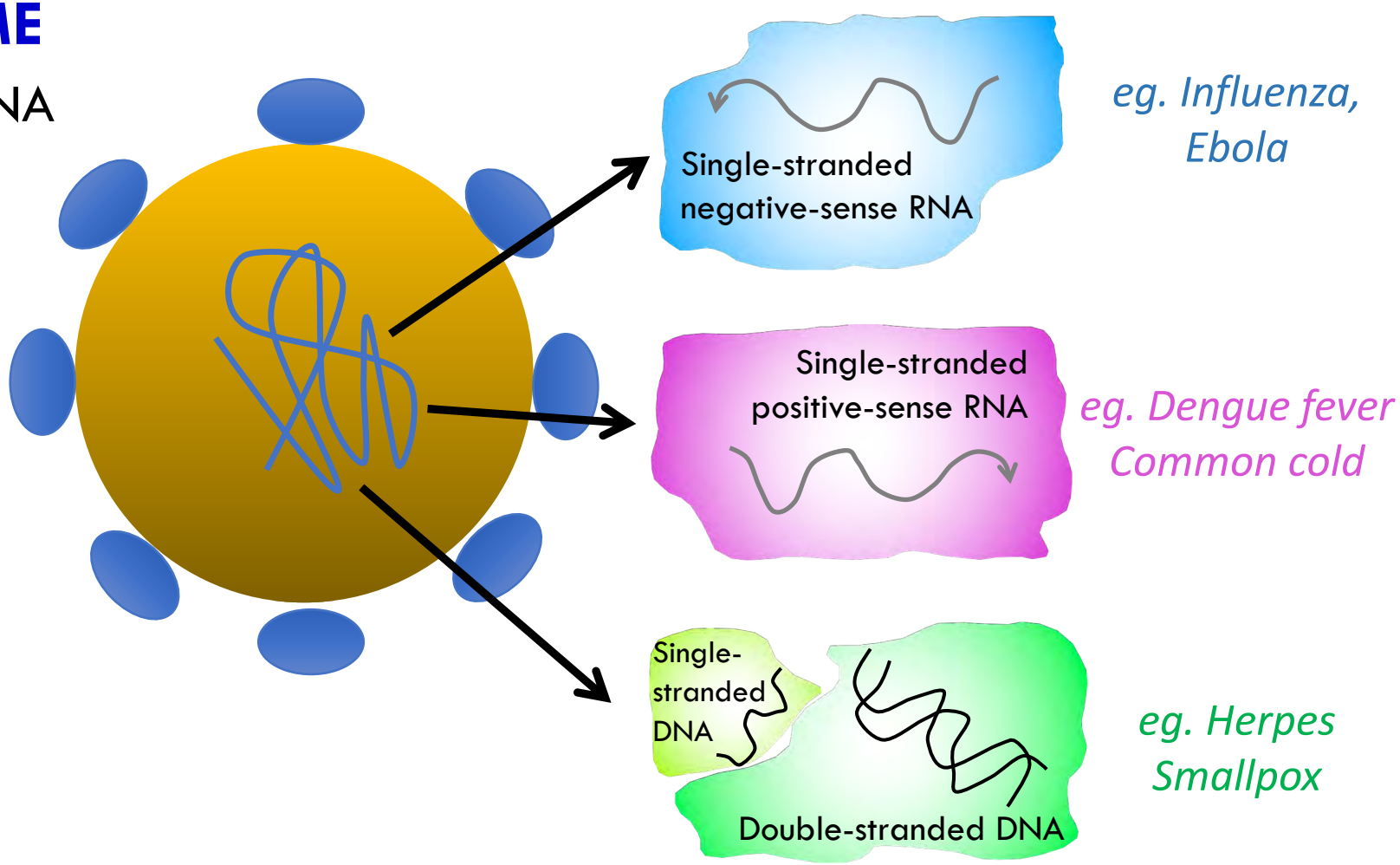
RNA or DNA

RNA:

Ribo**N**ucleic **A**cid

DNA:

Deoxyribo**N**ucleic **A**cid



Honey bee viruses

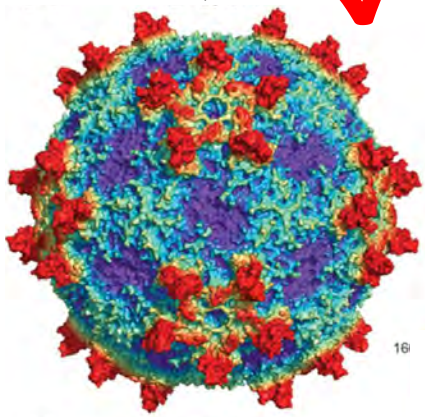
+ Lake Sinai Virus 1 and 2 ✓

- Historically ~24 viruses
- Australia has 5 common viruses
- **New viruses** being discovered

Black queen cell virus

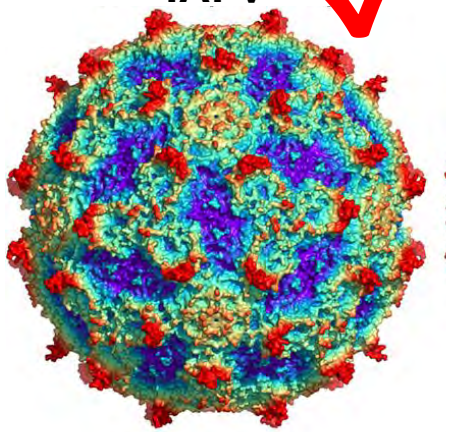
Sacbrood virus

BQCV ✓



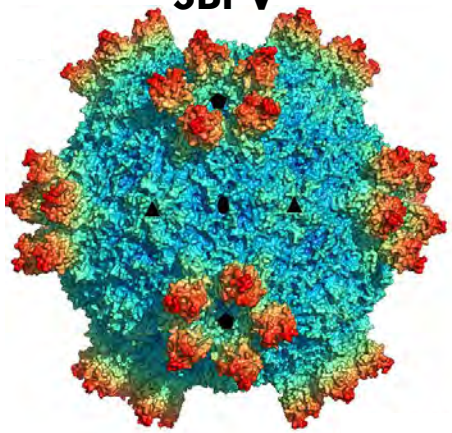
Black queen cell virus

IAPV ✓



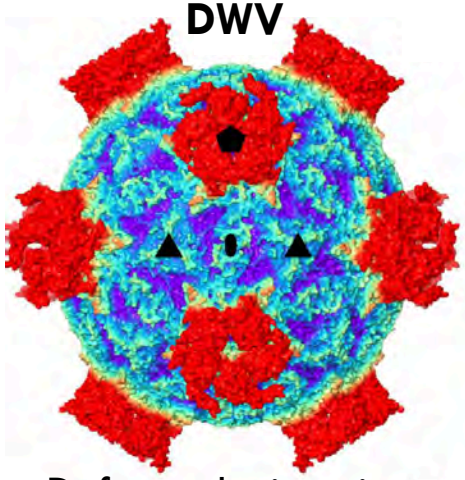
Israeli acute paralysis virus

SBPV



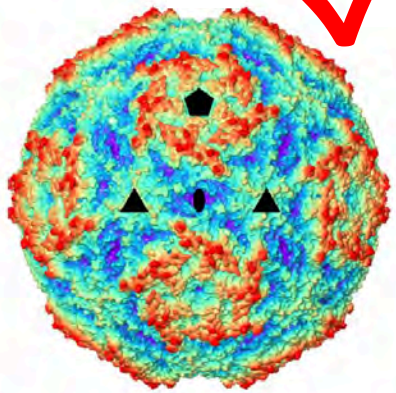
Slow bee paralysis virus

DWV



Deformed wing virus

SBV ✓

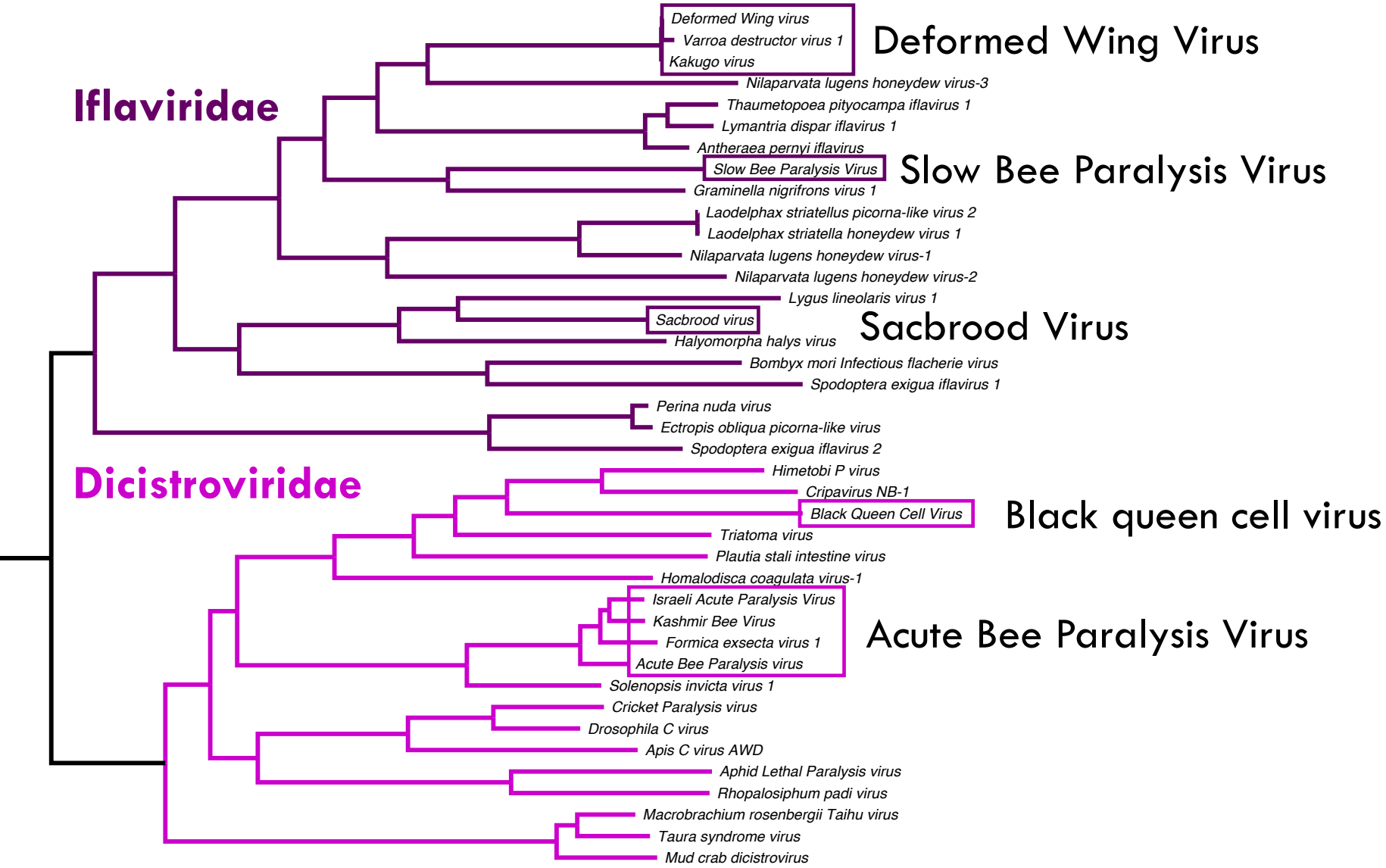


Sacbrood virus

Spurny et al **2017** J Virol 91(6); Prochazkova et al **2018** PNAS 115(30); Škubník et al **2017** PNAS 114(12); Kalynych et al, **2016** J Virol 90(16); Mullapudi, et al, **2016** J Virol 90(18)

Honey bee viruses

Single-stranded positive-sense RNA



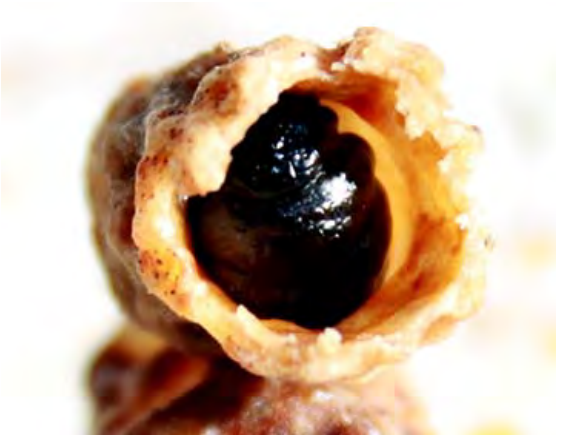
Deformed Wing Virus

Slow Bee Paralysis Virus

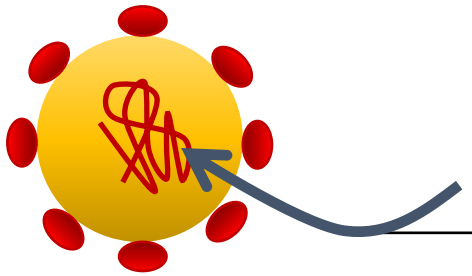
Sacbrood Virus

Black queen cell virus

Acute Bee Paralysis Virus



Virus Classification



Genome type	Honey bees	Insects
Single-stranded negative-sense RNA		✓
Single-stranded positive-sense RNA		✓
Single-stranded DNA; Double-stranded DNA		✓

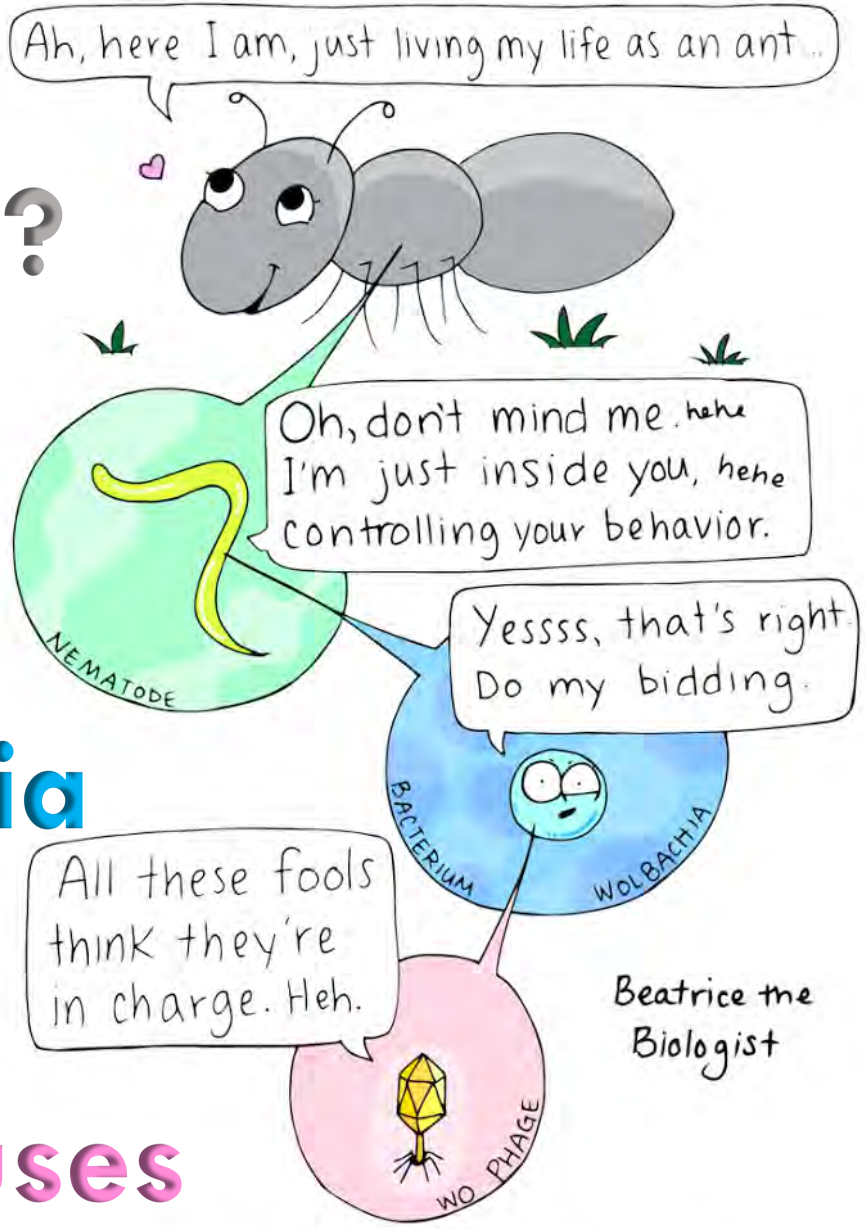
Who's really in control?

Us?

Parasites

Bacteria

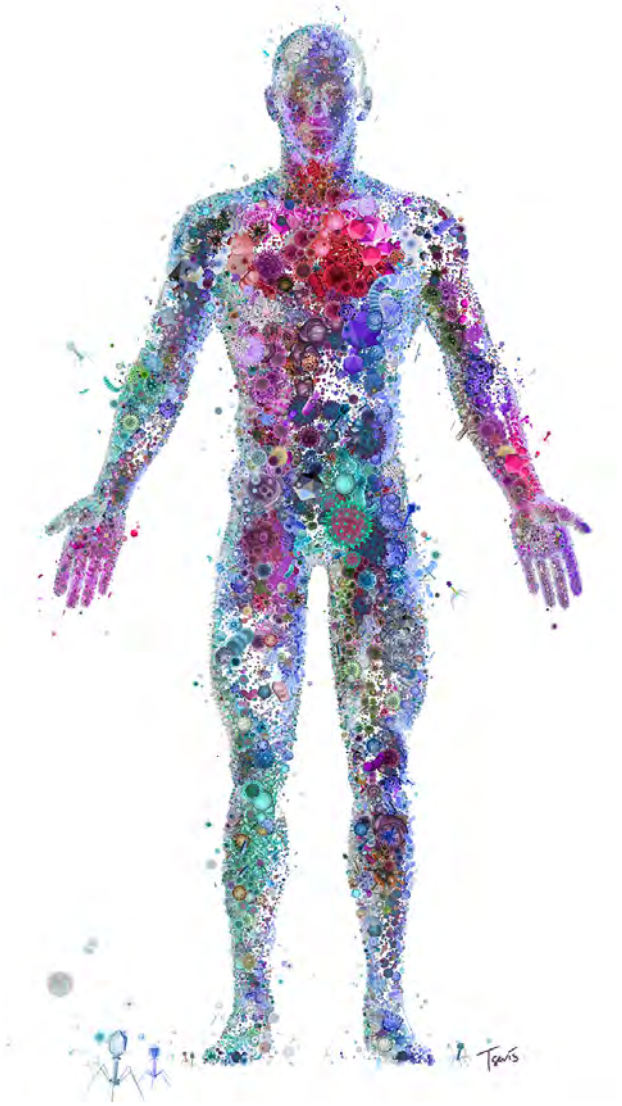
Viruses



Concept by Dr. Mark Martin, University of Puget Sound

The Microbiome

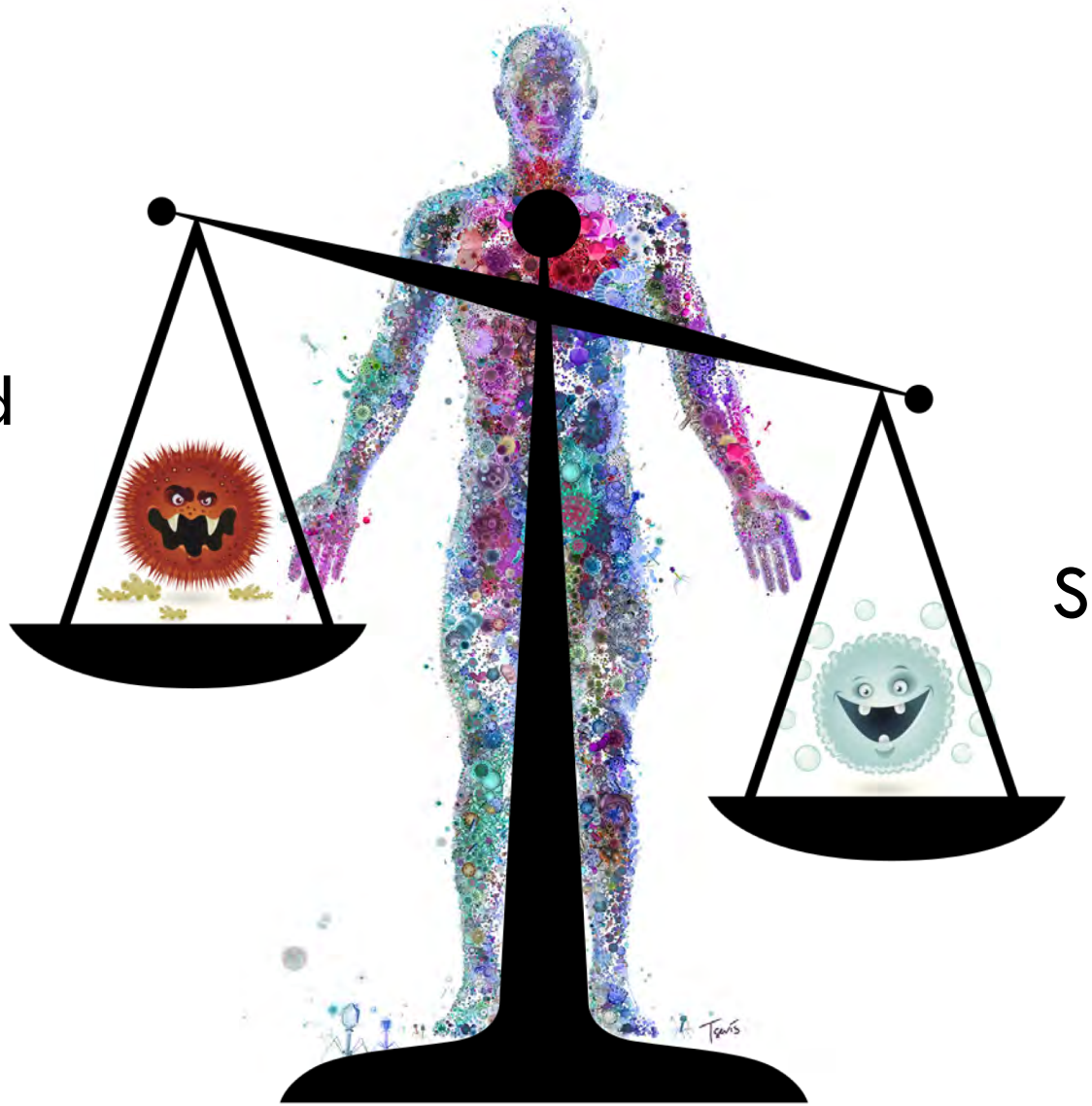
We are FULL of microorganisms



that impact how our body works

The Microbiome

Some Bad



Some Good

Feeling lonely?

Just remember,
you're not alone.

YOU ARE NEVER ALONE.

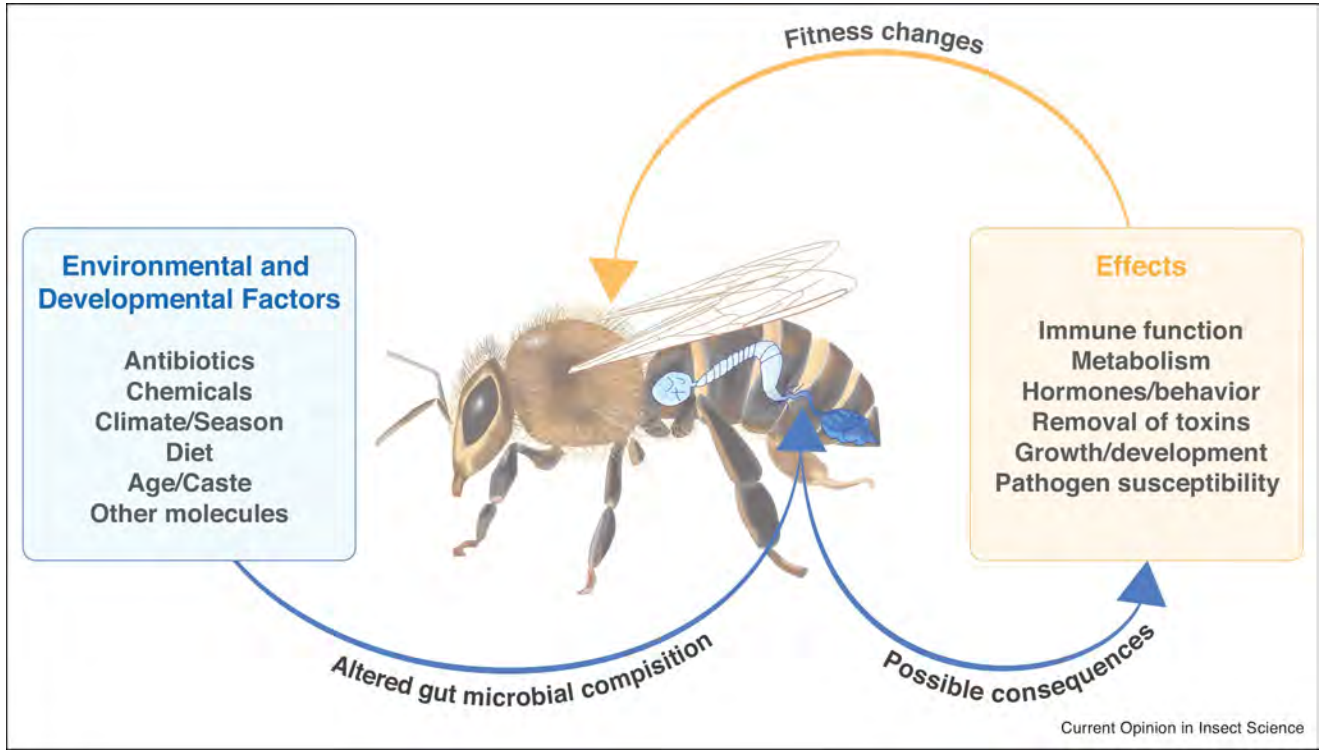
birdandmoon.com

What's living inside our bees?

The good, the bad and the ugly

The bee gut

- 8-10 core species of bacteria in the gut, with key roles in health and development



Honey bee diseases

VIRUSES

Deformed wing
Kakugo
Black Queen Cell
Sacbrood
Cloudy wing
Israeli Acute Paralysis
Kashmir Bee
Acute Paralysis
Chronic Paralysis
Slow paralysis
etc……

FUNGI

Nosema
Chalkbrood

BACTERIA

American foulbrood
European foulbrood


THE
UGLY

Arrival of a new* pest

Varroa destructor: Parasitic mite

Jumped from *Apis cerana* → *Apis mellifera*

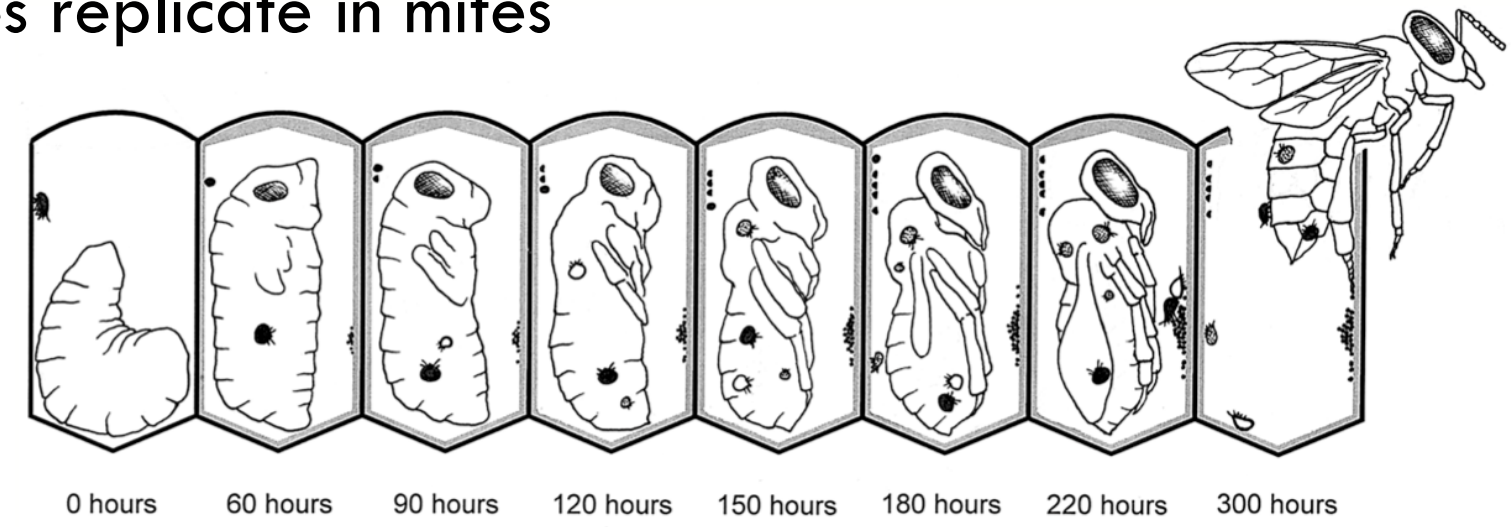
Apis cerana
Asian honey bee

Apis mellifera
European honey bee

National Geographic Japan; https://www.youtube.com/watch?v=lMtFYt7ko_o

Impact of *Varroa*

- Wounding and weakening
  - Damage to the cuticle
  - Feeds on developing bees
- Vector for viruses
  - Spreads viruses
  - Viruses replicate in mites



We're *still* learning about *Varroa*…

HOT OFF THE PRESS!!

- *Varroa* feeds on the bee's **fat body,** *not* **haemolymph** ('bee blood')
- The **genome** of *Varroa* has been sequenced

Ramsey, S. D., et al, (2019). *Varroa destructor feeds primarily on honey bee fat body tissue and not hemolymph.* PNAS **116**(5): 1792-1801

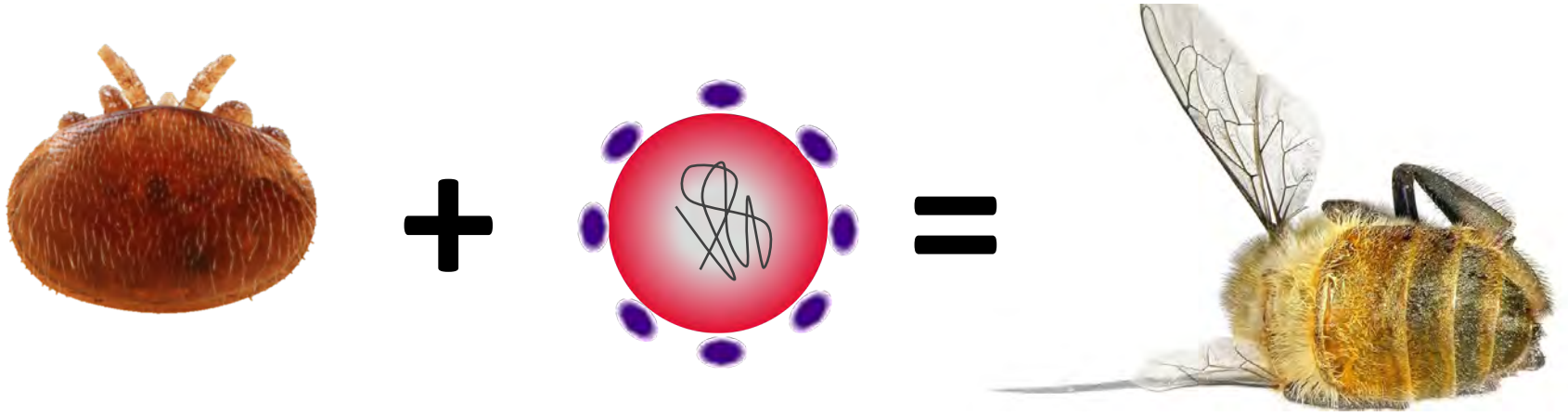
Bees brought to their knees

Viruses have changed since the arrival of *Varroa*

The main suspect: **Deformed wing virus (DWV)**

- *Varroa* arrives: DWV levels rapidly increase
- Left untreated for mites, hives die in 2-3 years

Deformed wing virus: Global pandemic



Global Honey Bee Viral Landscape Altered by a Parasitic Mite

Stephen J. Martin,[1]* Andrea C. Highfield,[2] Laura Brettell,[1] Ethel M. Villalobos,[3] Giles E. Budge,[4] Michelle Powell,[4] Scott Nikaido,[3] Declan C. Schroeder[2]*

8 JUNE 2012 VOL 336 SCIENCE

HONEYBEE DISEASE

Deformed wing virus is a recent global epidemic in honeybees driven by *Varroa* mites

5 FEBRUARY 2016 • VOL 351 ISSUE 6273 sciencemag.org SCIENCE

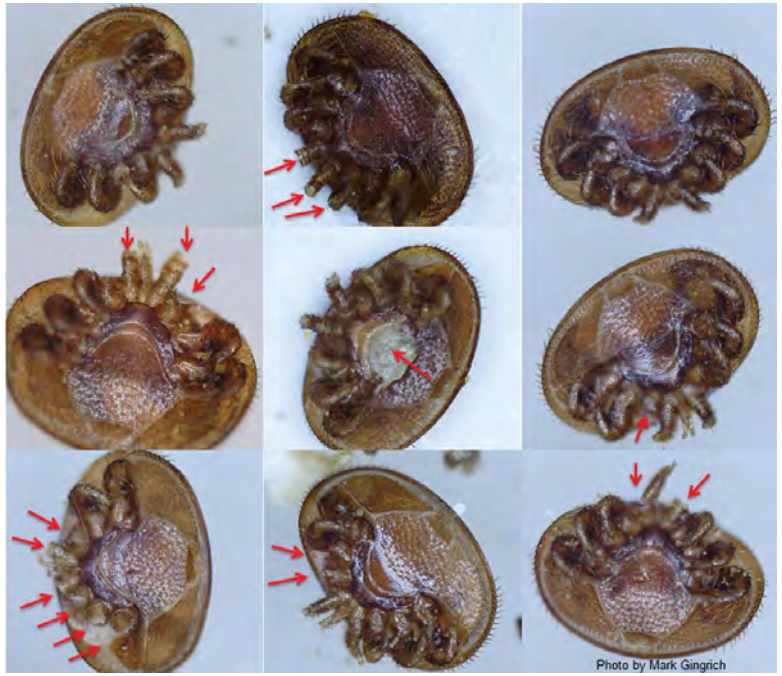
So how do we stop viruses?

…get rid of mites…?

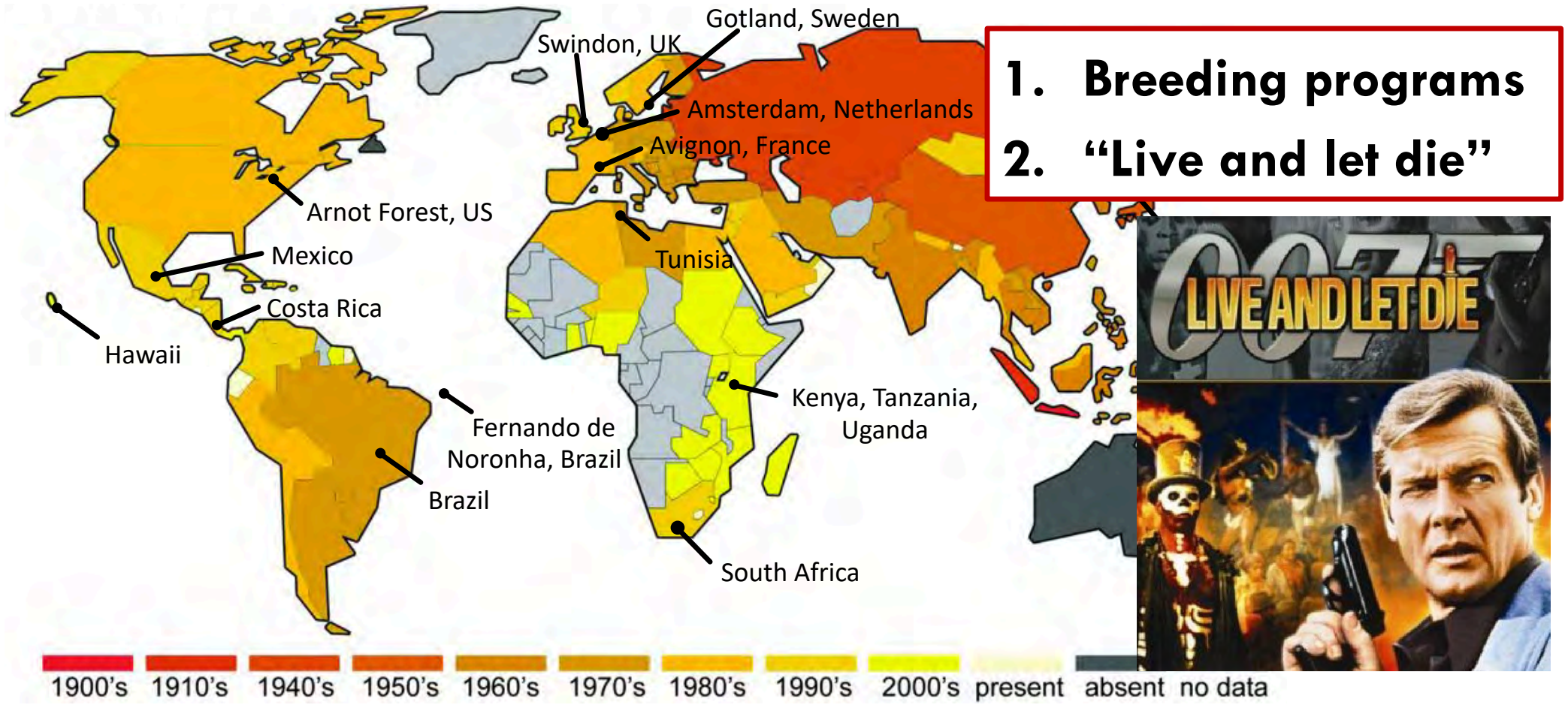
Ways to get rid of mites

- Chemical treatments
  - In hive residues, bad for bees
  - Mites can become resistant

- Natural selection of Varroa-tolerance or resistance
  - Over time, bees learn to live with, or get rid of, mites



Colonies can survive mite infestations without chemical intervention

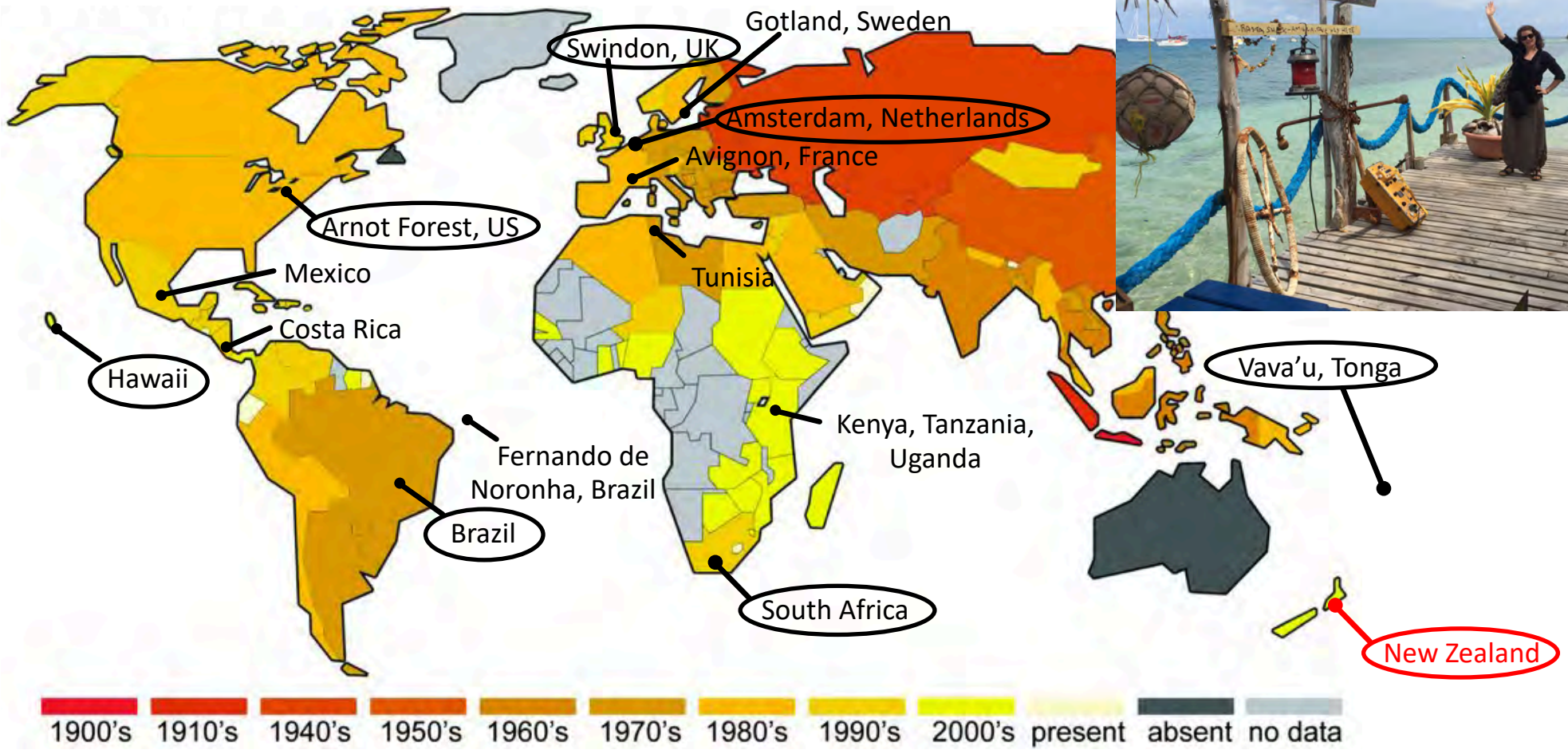


1. **Breeding programs**
2. **"Live and let die"**

Wilfert *et. al,* (2016) Deformed wing virus is a recent global epidemic in honeybees driven by *Varroa* mites. Science **351**(6273), pp. 594-7
Adapted from: Locke, B., **2015** *Natural Varroa mite-surviving Apis mellifera honeybee populations*. Apidologie**:** 47**:** 467-482.

But are there still viruses in bees that tolerate *Varroa*?

Colonies can survive mite infestations without chemical intervention



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Adapted from: Locke, B., **2015** *Natural Varroa mite-surviving Apis mellifera honeybee populations*. Apidologie: *47*: 467-482.

Finding Bees

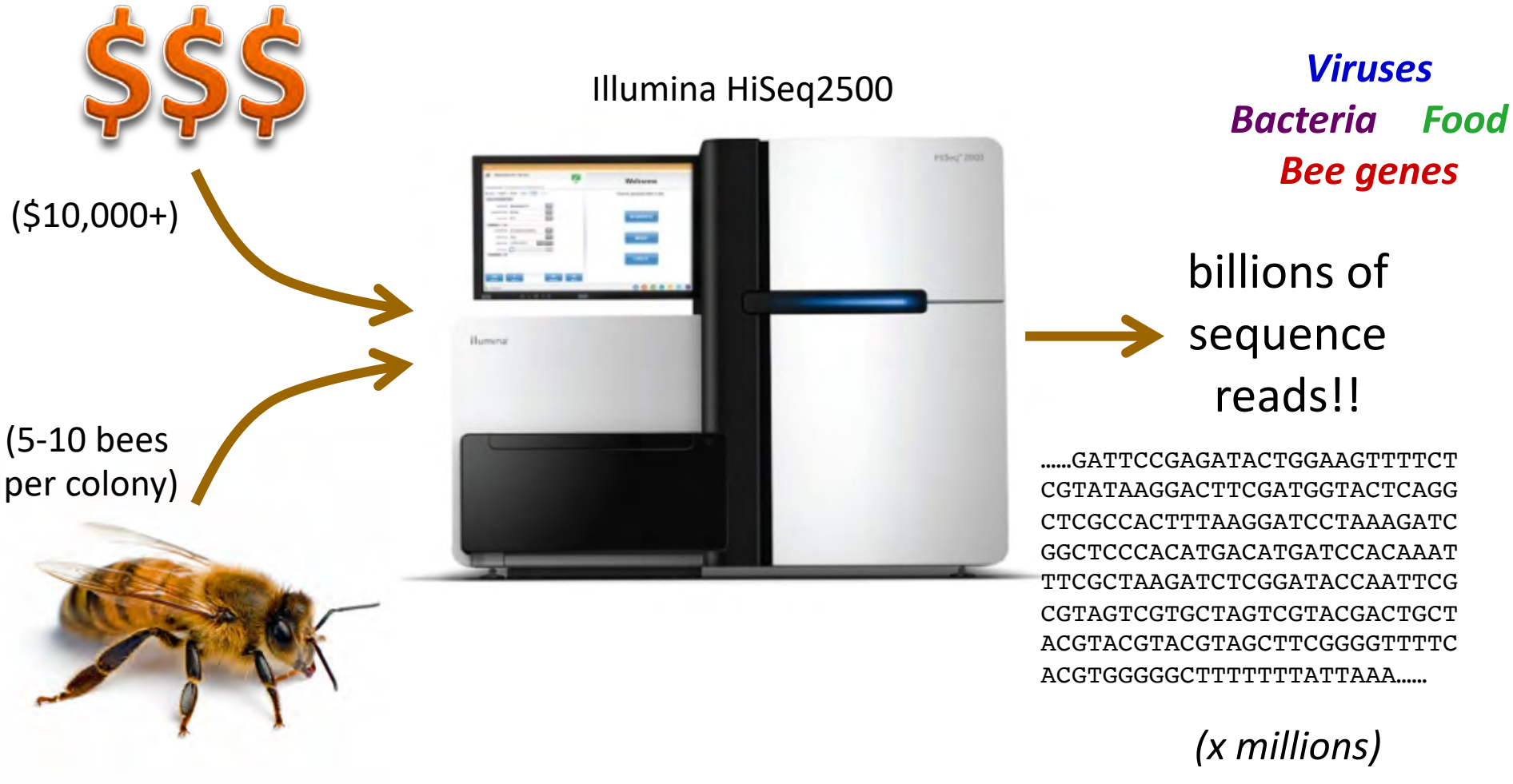

invitrogen


RNase
321-63-

Quarantine Approved Facility

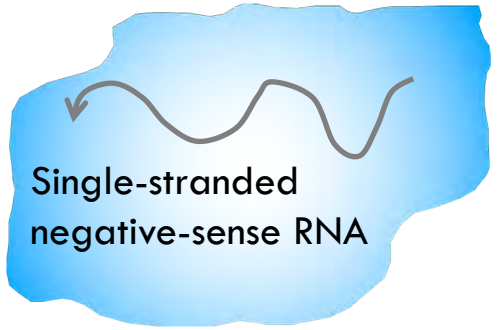
- Samples are imported frozen, stored at -80° until required
- No infected materials leave the quarantine areas of the lab
- Samples are denatured, non-infectious, non-viable derivatives
- Waste is autoclaved and disposed of according to quarantine approved protocols

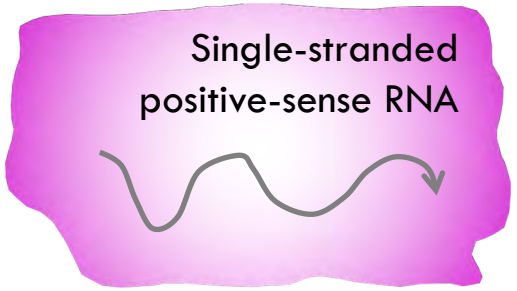
Sequence all the genetic material inside a bee



7 new RNA viruses

First negative sense RNA viruses in bees

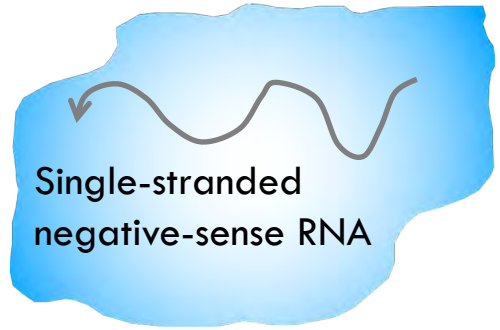




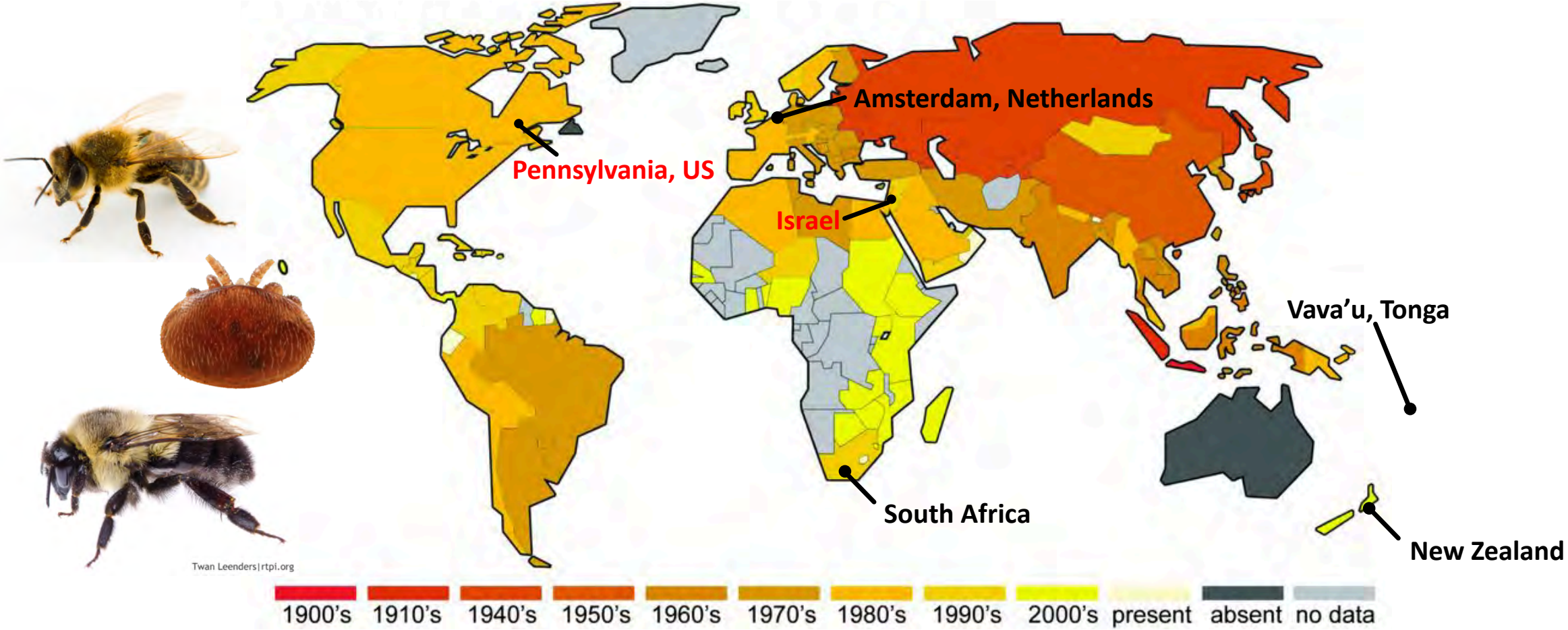
	Netherlands	South Africa	Tonga	New Zealand
Apis Rhabdovirus 1	✓	✓	✓	✓
Apis Rhabdovirus 2	✓	✓	✓	✓
Apis Bunyavirus 1		✓		
Apis Bunyavirus 2		✓		
Apis C virus	✓			
Apis Flavivirus		✓		
Apis Nora virus		✓		

Remnant *et. al., (2017)* J Virol

Apis Rhabdovirus 1

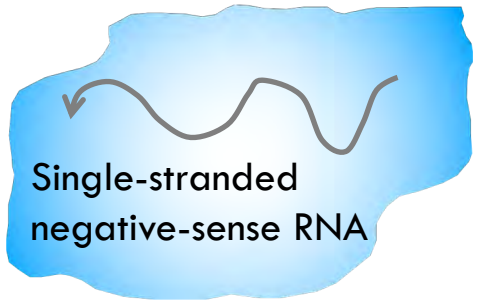
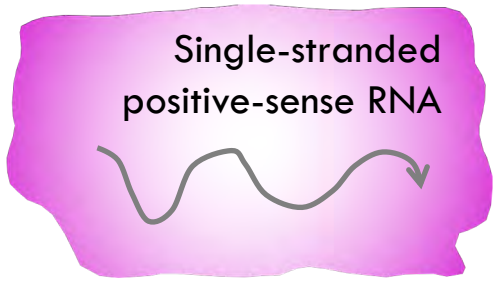
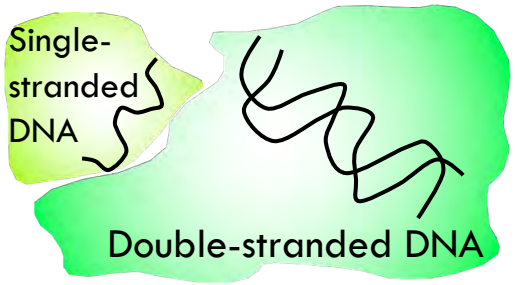


Geographically widespread, multi-host virus



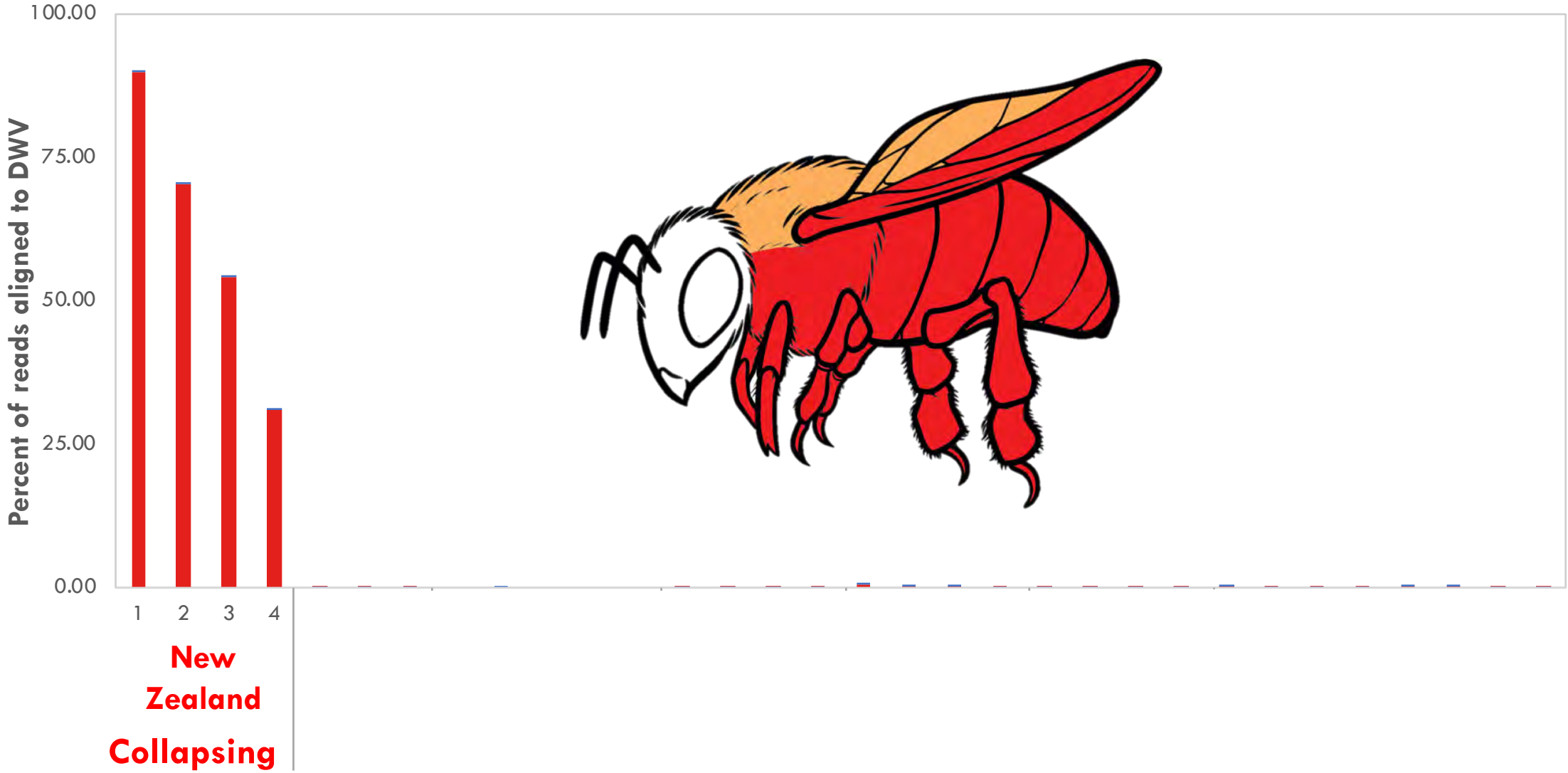
Remnant *et. al., (2017)* Journal of Virology, 91(16); Levin *et. al., (2017)* Frontiers in Microbiology, 8(2482)

Virus Classification

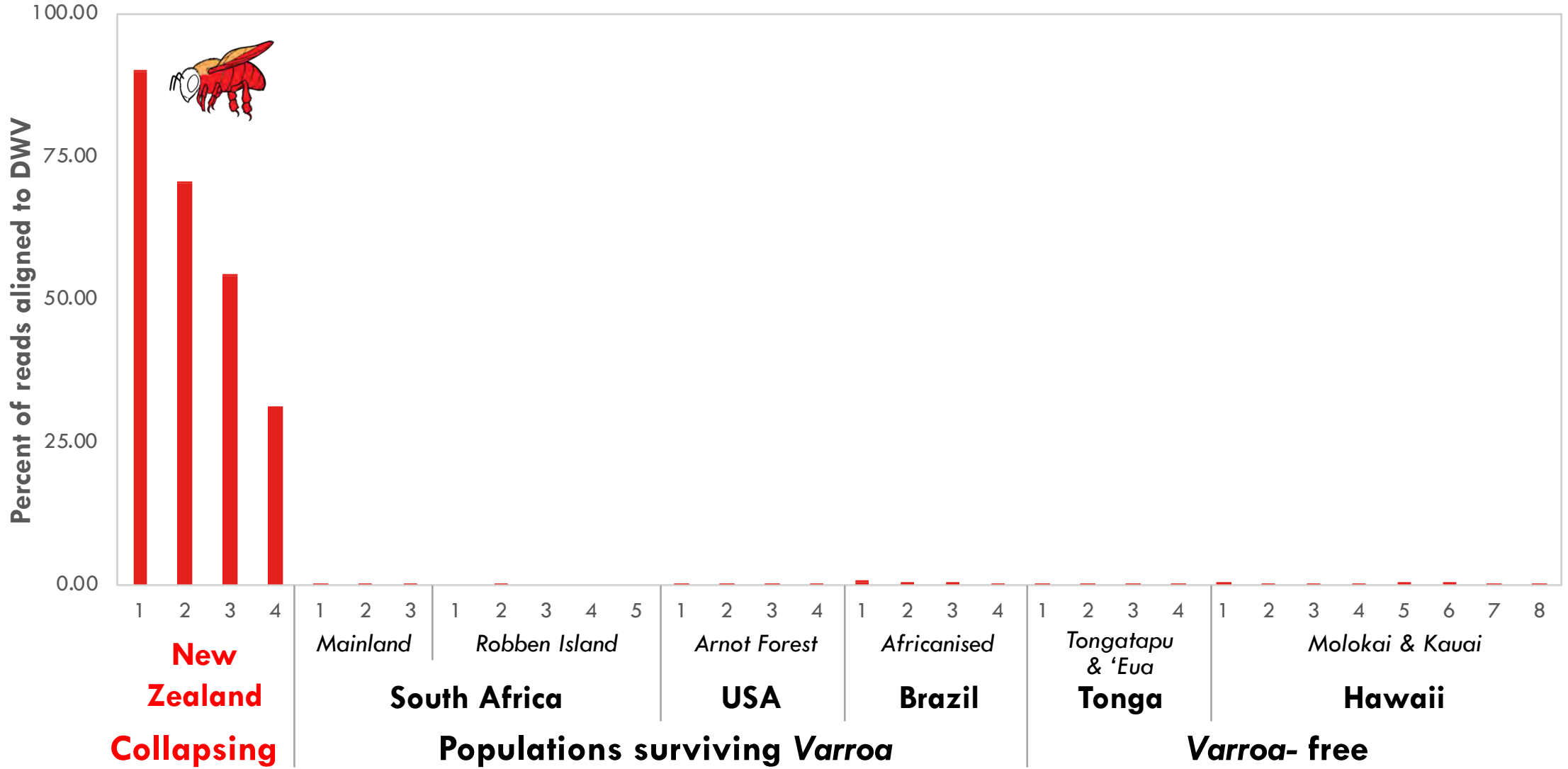
Genome type	Honey bees	Insects
	4	✓
	25	✓
	2	✓

We don't know what the new viruses do

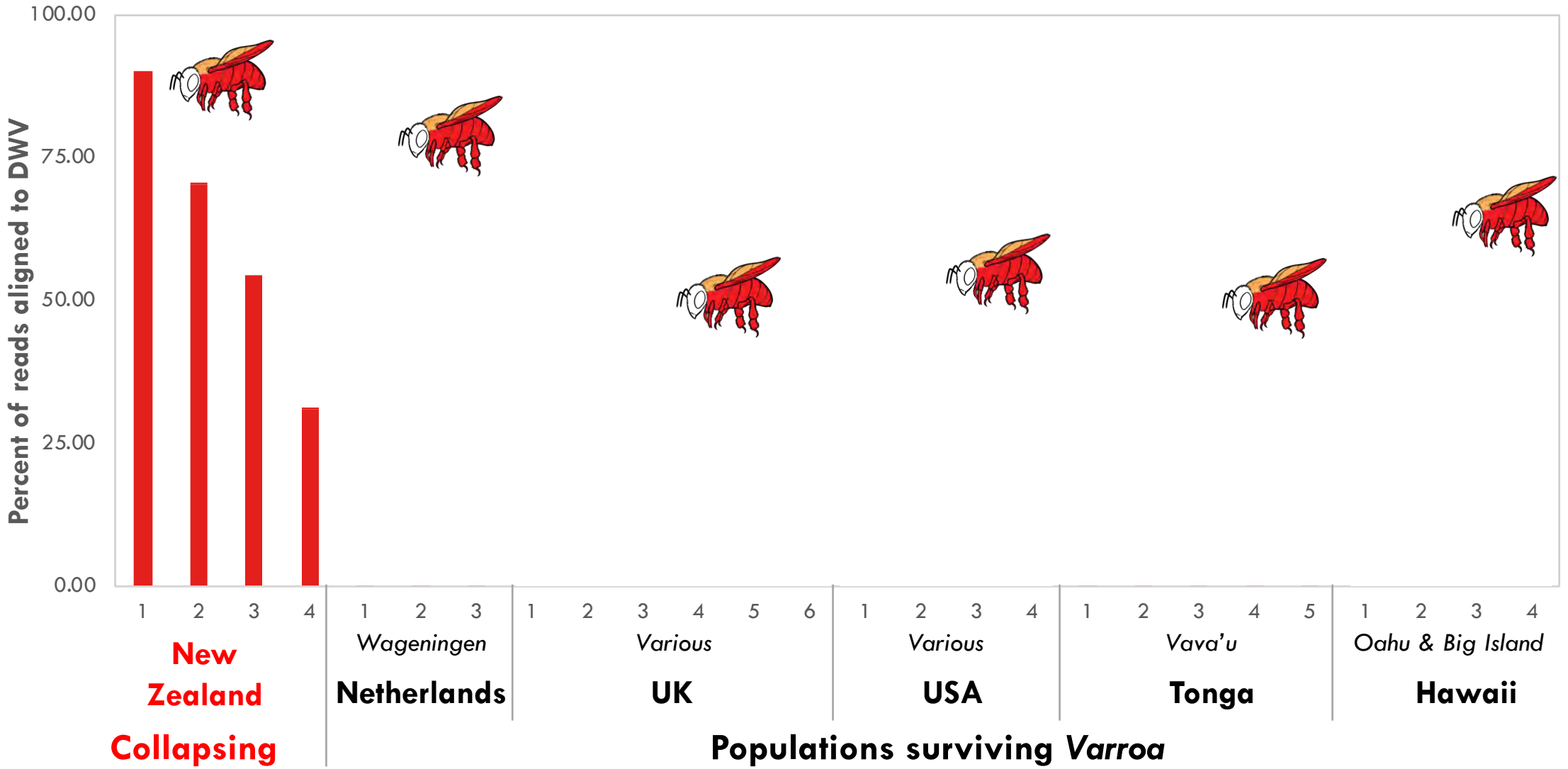
Virus levels in bees can be pretty high!



DWV is absent in some populations surviving *Varroa*



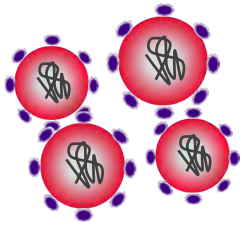
High levels of DWV in other populations surviving *Varroa*

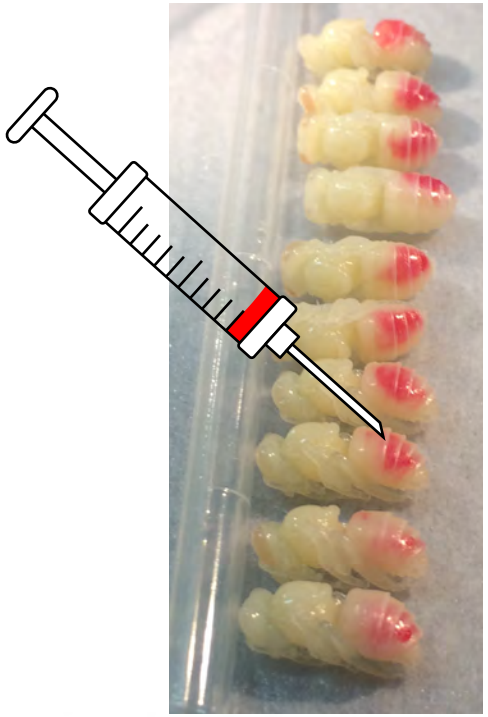


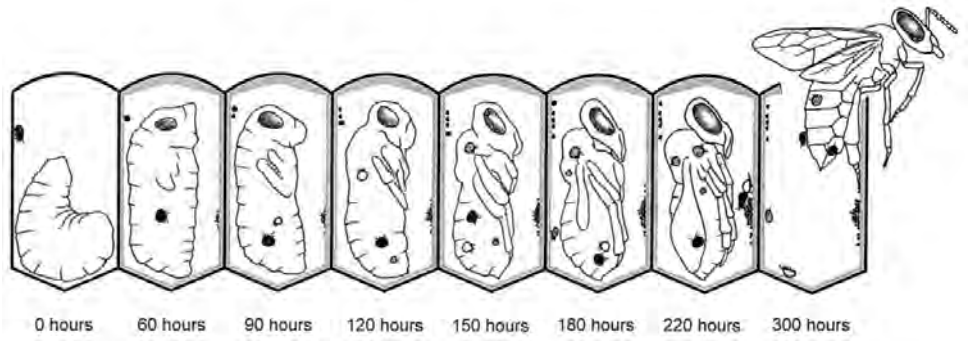
What can we do about it?

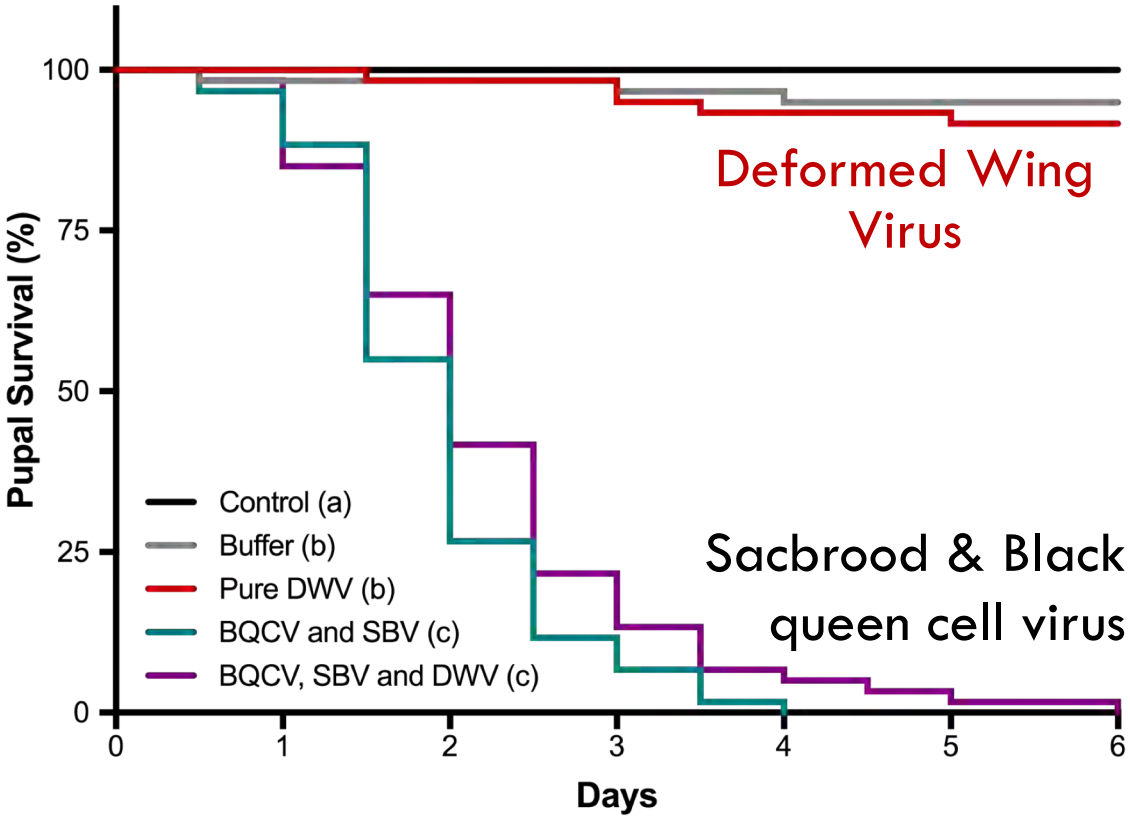
- *Varroa* has increased Deformed wing virus levels in bees
  - Is that a bad thing?

Should we be worried about Deformed Wing Virus?









DWV allows pupal survival and adult emergence

Remnant *et. al.* (2019). *Direct transmission by injection affects competition among RNA viruses in honeybees* Proc B **286**(1895): 20182452.

What can we do about it?

- *Varroa* has increased Deformed wing virus levels in bees
  - Is that a bad thing? – ***PROBABLY not a good thing…***
  - Long term effects on colony survival

- Impact of viruses remains high in most places
  - ***Varroa*-resistance** may not be a complete solution
  - Can we reduce virus levels in bees by other mechanisms?

Meanwhile, in other insects…

OPEN ACCESS Freely available online

PLOS BIOLOGY

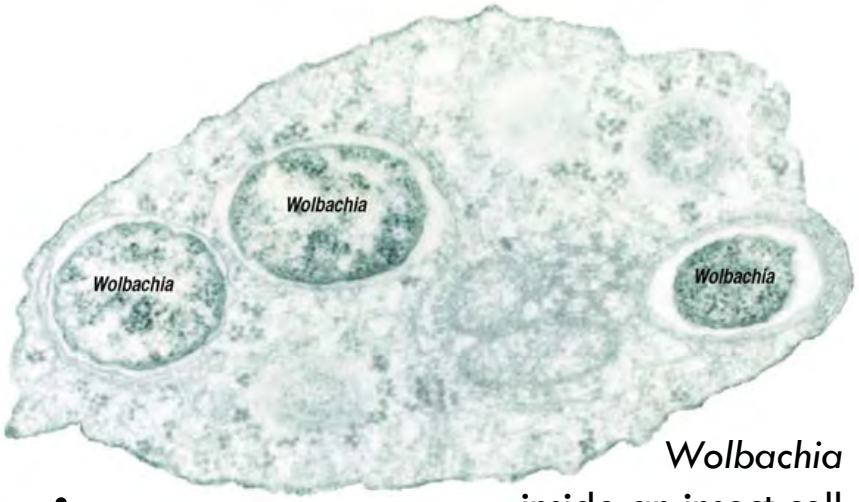
The Bacterial Symbiont *Wolbachia* Induces Resistance to RNA Viral Infections in *Drosophila melanogaster*

Luís Teixeira*, Álvaro Ferreira, Michael Ashburner

Department of Genetics, University of Cambridge, Cambridge, United Kingdom

What is Wolbachia?

Wolbachia pipientis



Wolbachia inside an insect cell

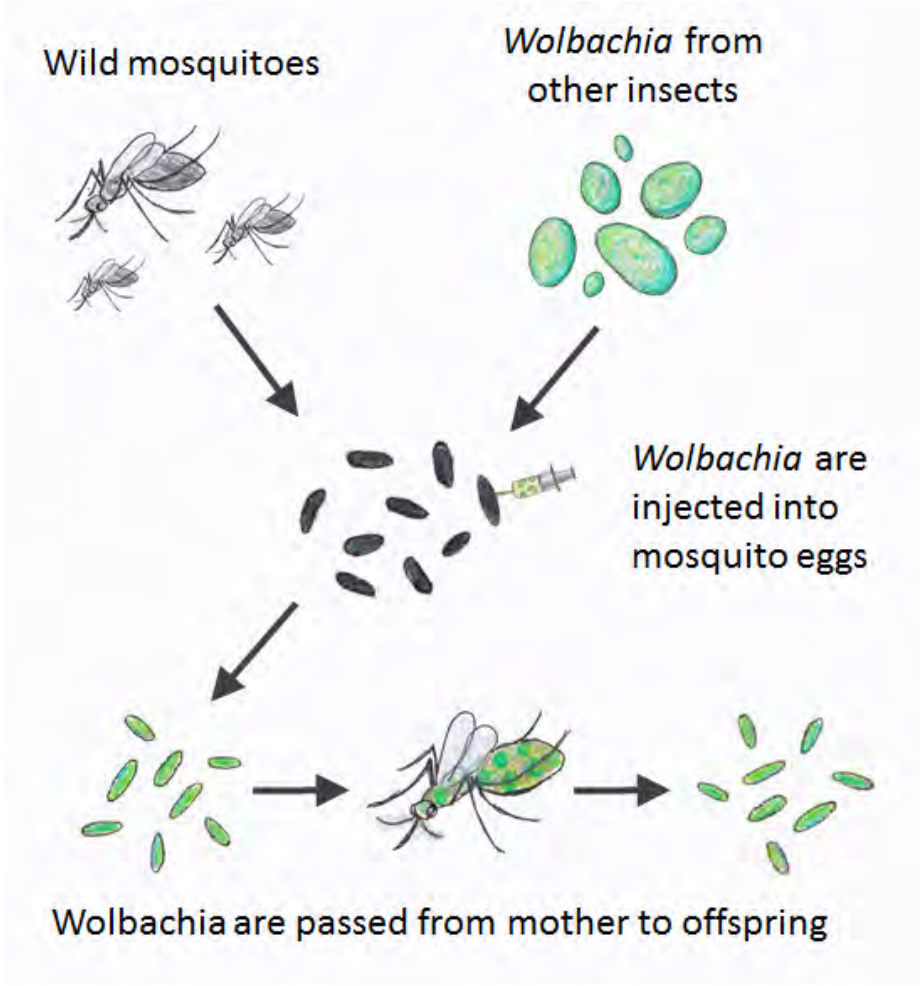
- Bacteria that lives inside cells
- Infects about half of all insect species
- Manipulates insect hosts to increase transmission
- Provides **resistance to viruses** in flies and mosquitoes

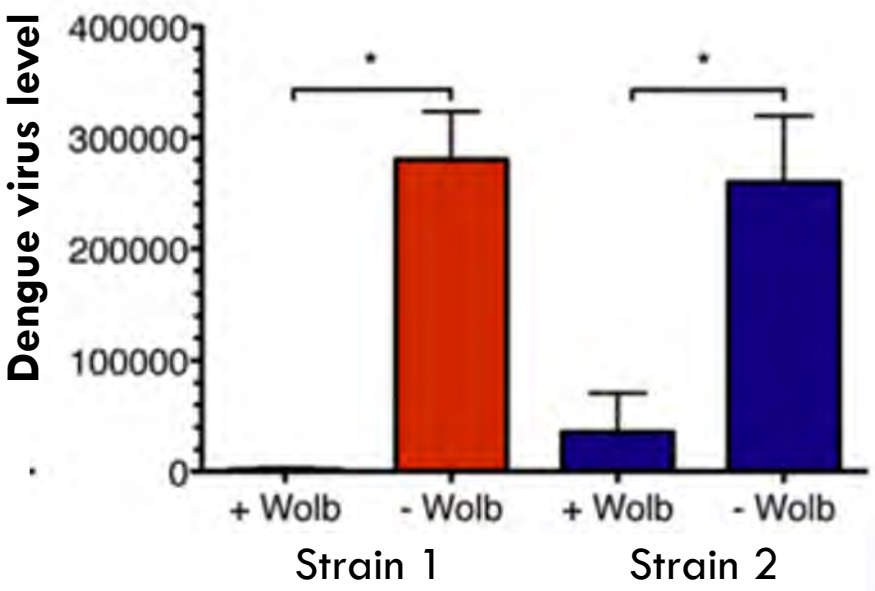
ELIMINATE DENGUE™
OUR CHALLENGE

'Eliminate Dengue'

- Dengue fever: WHO #1 mosquito-borne disease
  - 30-fold increase in past 10 years
- *Aedes aegypti* mosquito:
  - vector of Dengue, Chikungunya, Zika virus
- Use a natural mechanism to prevent spread of Dengue fever: infect mosquitoes with *Wolbachia*

The Wolbachia method



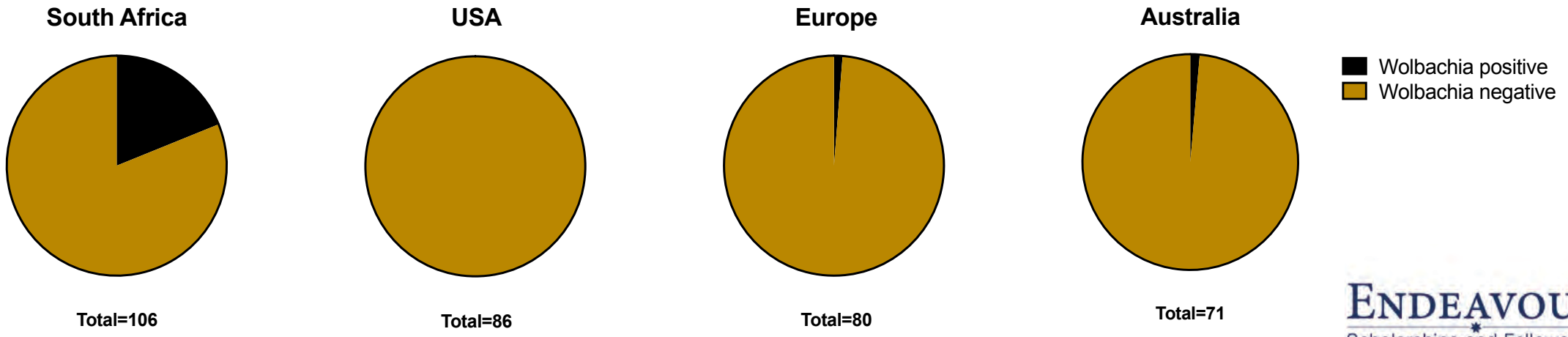


Images: Perran Ross

Moreira, L. A., et al, (2009). "A *Wolbachia* symbiont in *Aedes aegypti* limits infection with Dengue, Chikungunya, and *Plasmodium*." Cell **139**(7): 1268-1278.

Wolbachia in bees?

- Present in African honey bee subspecies- *these bees had low virus levels*
- Little evidence for *Wolbachia* elsewhere in *Apis*
  - Antibiotic treatments will remove *Wolbachia*



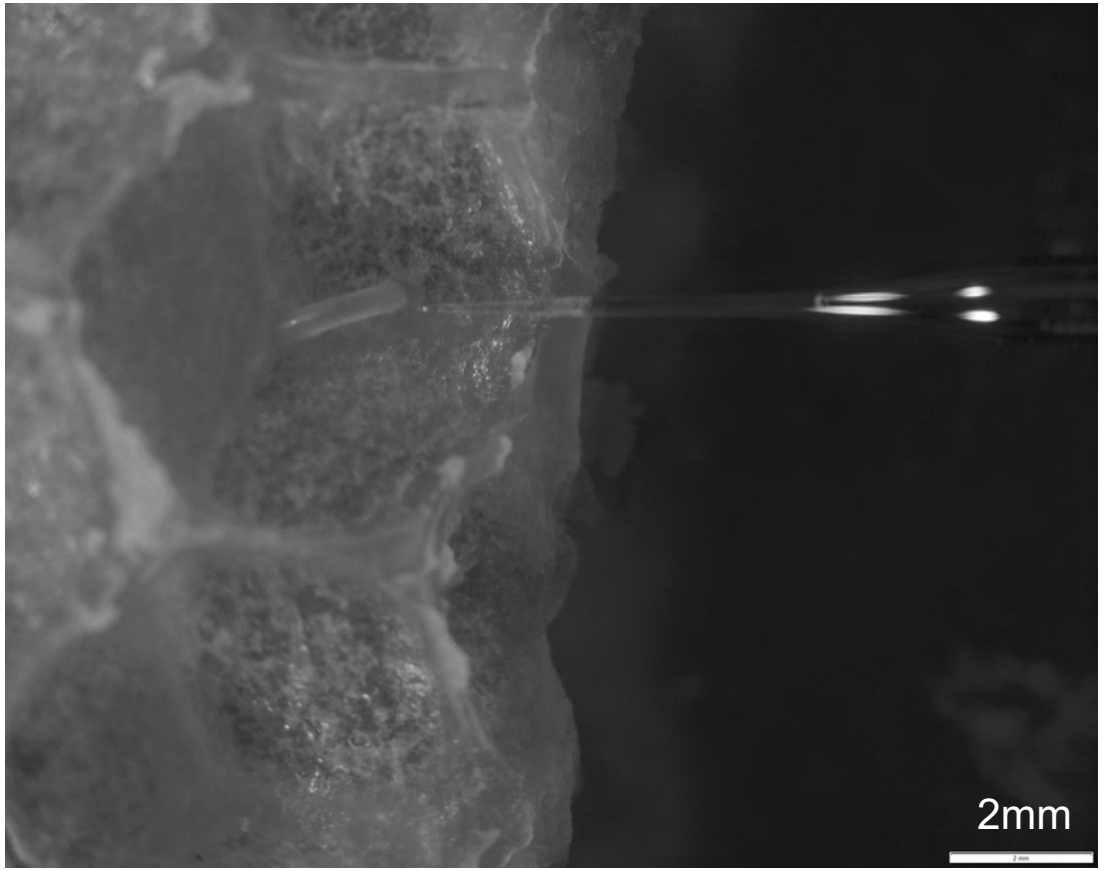
Can *Wolbachia* provide virus resistance to honey bees?

Can we immunise honey bees with bacteria?

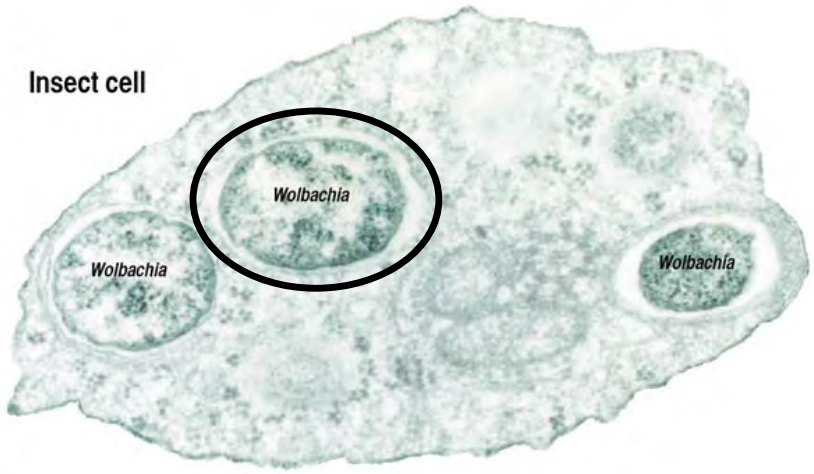
Wolbachia experiments:

- Contained in our quarantine lab
- Microinjection wolbachia into honey bee eggs and queen pupae → ovaries
  - Does it survive?
  - Does it reduce viruses?

WATCH THIS SPACE!



Can we reduce viruses in honey bees with bacteria?



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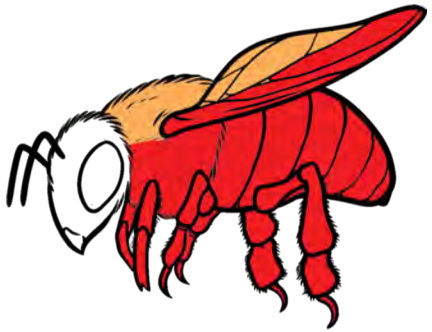

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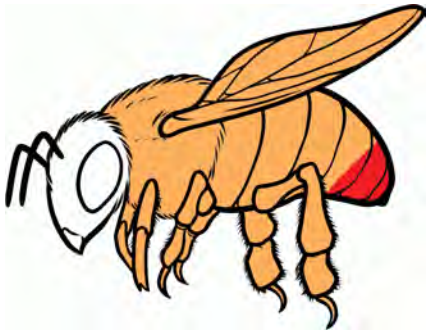

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OUR CHALLENGE

The power and promise of genomics for honey bee health:

- Virus **levels, strains** and **new viruses** identified
- ***Varroa*-resistant** bee populations have different viruses
- What genes do bees use protect themselves against viruses?
- **Can we use protective bacteria to reduce viruses in bees?**

Working towards new strategies for disease diagnosis and control

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Thanks for listening!

Questions? Comments? Ideas?

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