Evolutionary ecology of the dynamics of antibodies

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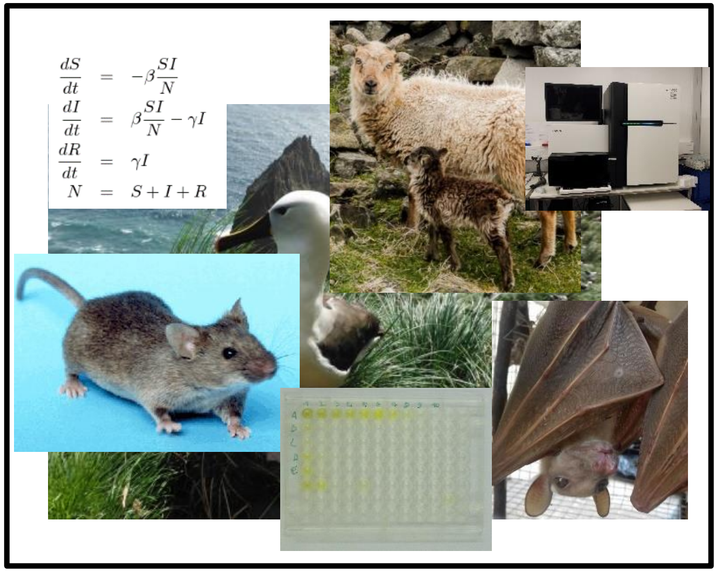
Wild Immunology

Why should we care about the **dynamics** of immunity?

Strain diversity
Resistance and tolerance

EVOLUTION



ECOLOGY

Life history
Contacts

EPIDEMIOLOGY

Source of infection
Spatial aspects

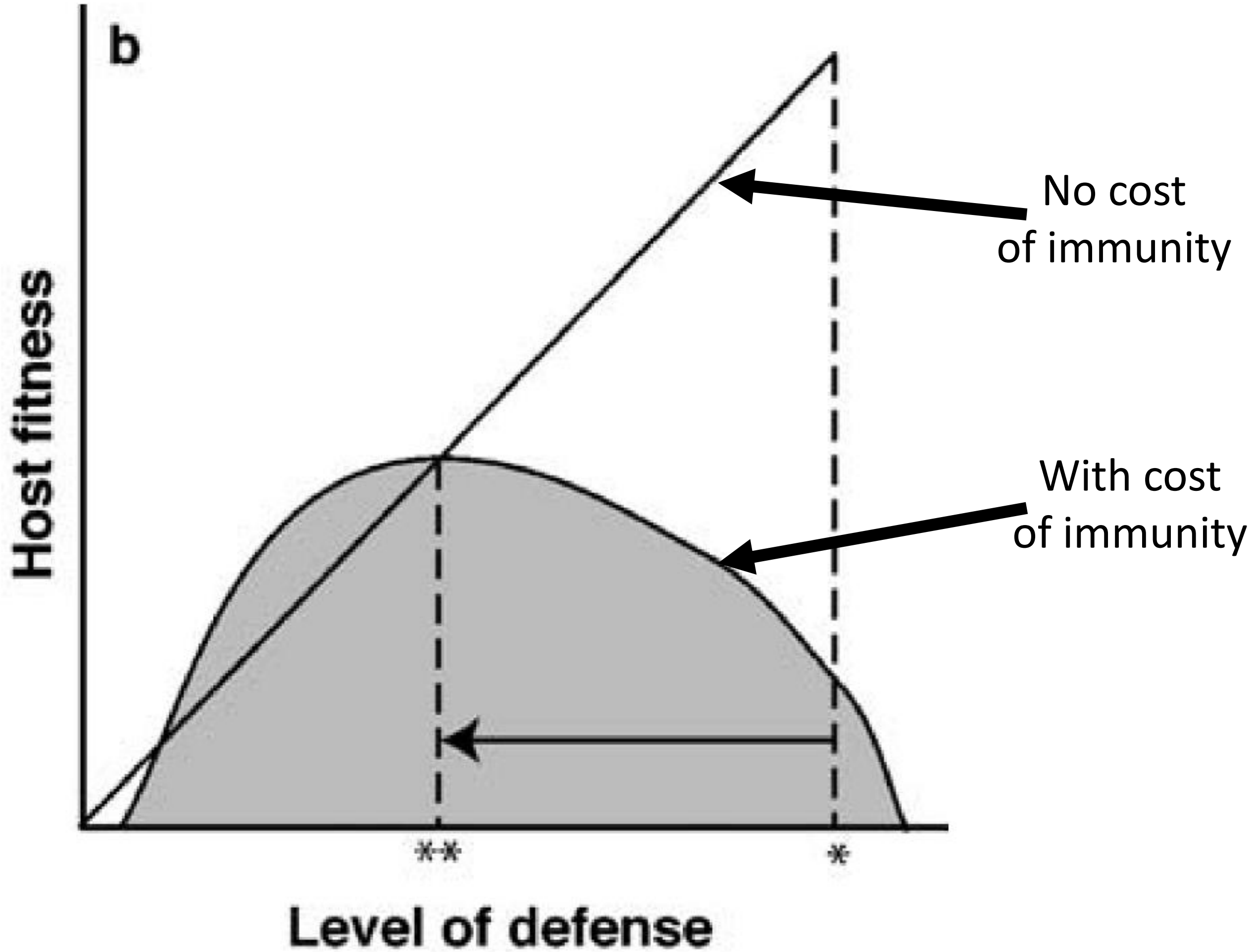
IMMUNOLOGY

Different classes of
antibodies

Wild Immunology

Immune responses are highly variable in the wild

Balance of costs and benefits relatively poorly understood



Graham et al., Annu. Rev. Ecol. Evol. Sys., 2005

Wild Immunology

Immune responses are highly variable in the wild

Balance of costs and benefits relatively poorly understood

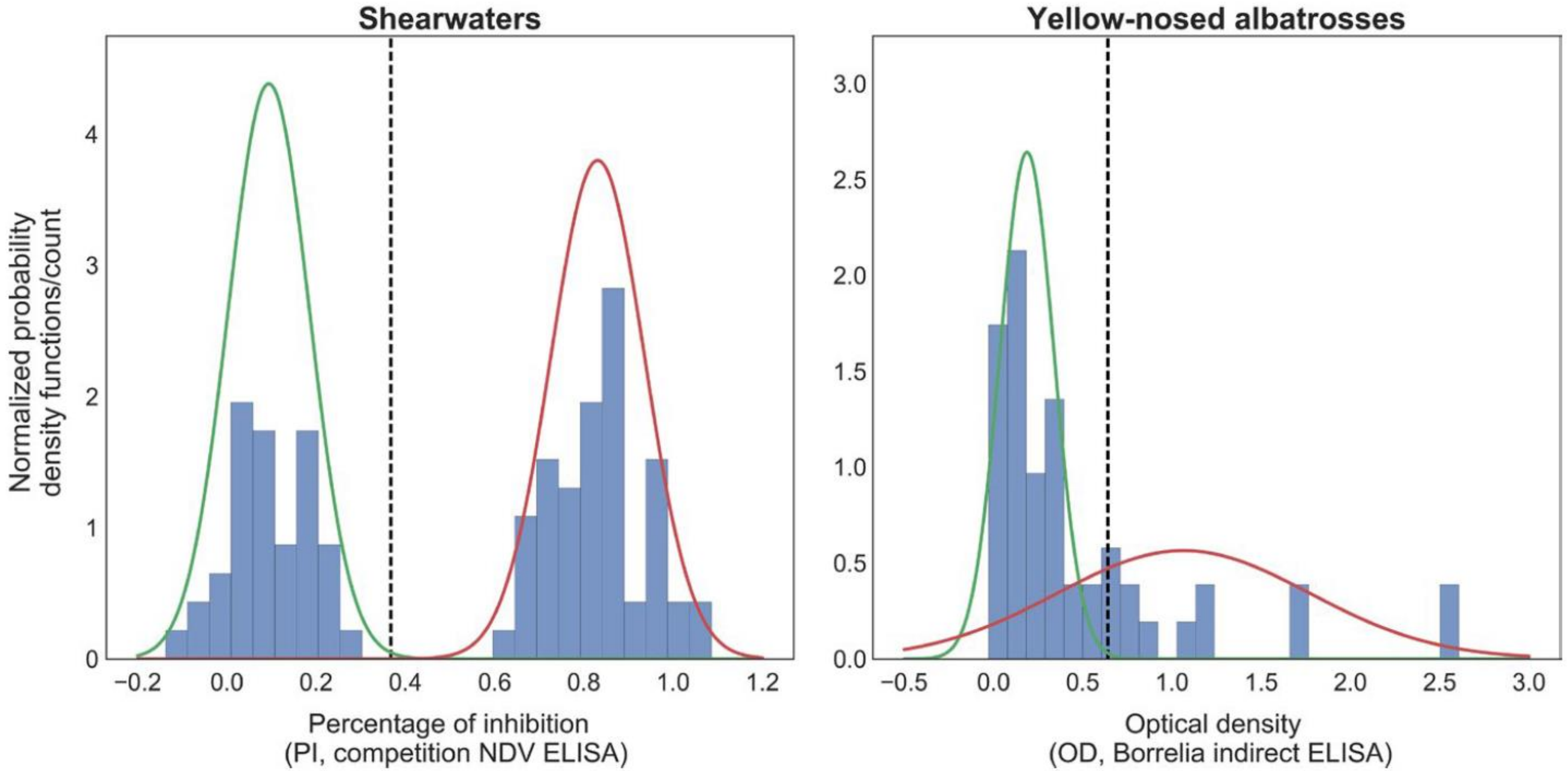
Ecological immunology still challenging

- Sampling – Adequate type? Quantity?
- Immune systems are highly dynamic
- Fitness relations of immune responses?
- Determining seropositivity?

Garnier and Graham, Int. Comp. Biol. 2014

Wild Immunology

Determining seropositivity – statistical approach



Mixture models to determine seropositivity cut-offs

Garnier et al., Func Ecol, 2017

Wild Immunology

Antibody dynamics increasingly accessible in wild animal populations because of the development of the serology toolbox

❶ **Ecology and dynamics of antibodies**

Dynamics of (maternal) antibodies and life history

❷ **Nutritional ecology and dynamics of antibodies**

Antibody, nutrition and fitness in a wild ungulate

❸ **Epidemiology and dynamics of antibodies**

Antibody dynamics to help predict bat-borne viruses spillover

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Ecology and dynamics of antibodies

Theoretical predictions:

Antibodies expected to provide longer protection to newborns of longer-lived species

Garnier et al., Evolution, 2012
Pigeault, Garnier, et al., Proc. Roy. Soc. B., 2016

Experimental vaccination in several species of seabirds against Newcastle Disease Virus

Long-lived Procellariiforms vs shorter-lived seabirds

Repeated sampling of chicks to estimate the half-life of IgY

Ecology and dynamics of antibodies

Longer half-life of IgY in Procellariiform species

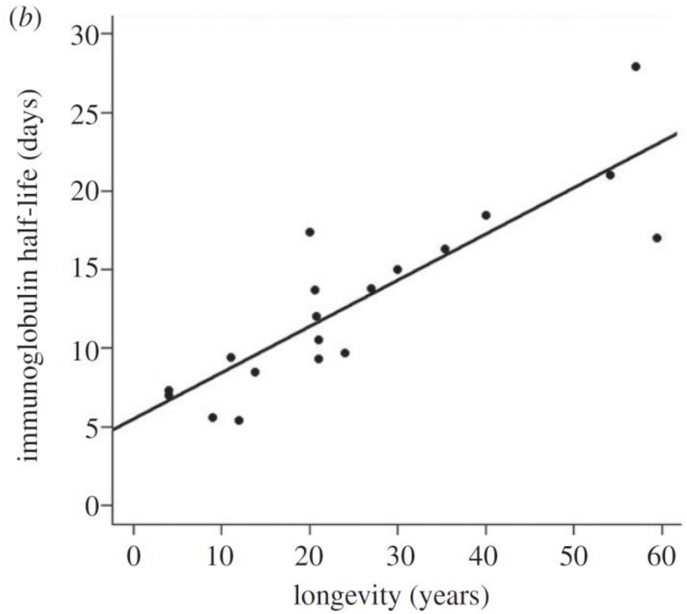
Garnier et al., Proc. Roy. Soc. B., 2012
Ramos, Garnier et al., in preparation

Ecology and dynamics of antibodies

Longer half-life of antibodies in slow-living Procellariiforms

- Mechanistic basis still unknown (IgY heavy chain? Recycling?)
- Need to include longer-lived non-Procellariiforms such as penguins

Similar lifespan/half-life association found in mammals.



Garnier et al., Biol. Lett., 2013

Evolutionary ecology and dynamics of antibodies

➊ **Ecology and dynamics of antibodies**

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Evolutionary ecology and dynamics of antibodies

Scarce evidence for indirect evidence for resource-based costs of immunity in wild animal population

Need to assess the correct immunological and nutritional currencies

Protein likely candidates as currency in ungulates of the Northern hemisphere

- Fat is the main energy resource during winter, but proteins are increasingly used when fat stores approach depletion
- Antibodies crucial for parasite control
- Albumin is the main protein for homeostasis
- Albumin and IgG physiologically linked through shared recycling mechanism

Evolutionary ecology and dynamics of antibodies

Positive association between albumin and IgG with possible fitness consequences

Higher levels of recycling receptors leading higher levels of both albumin and IgG

Trade-off immunity – nutrition may only be apparent after this association is taken into account

Need a population

- Well characterized role of parasites
- Parasite-specific immunity measurable
- Nutrition can be assessed
- Individual fitness known

Evolutionary ecology and dynamics of antibodies

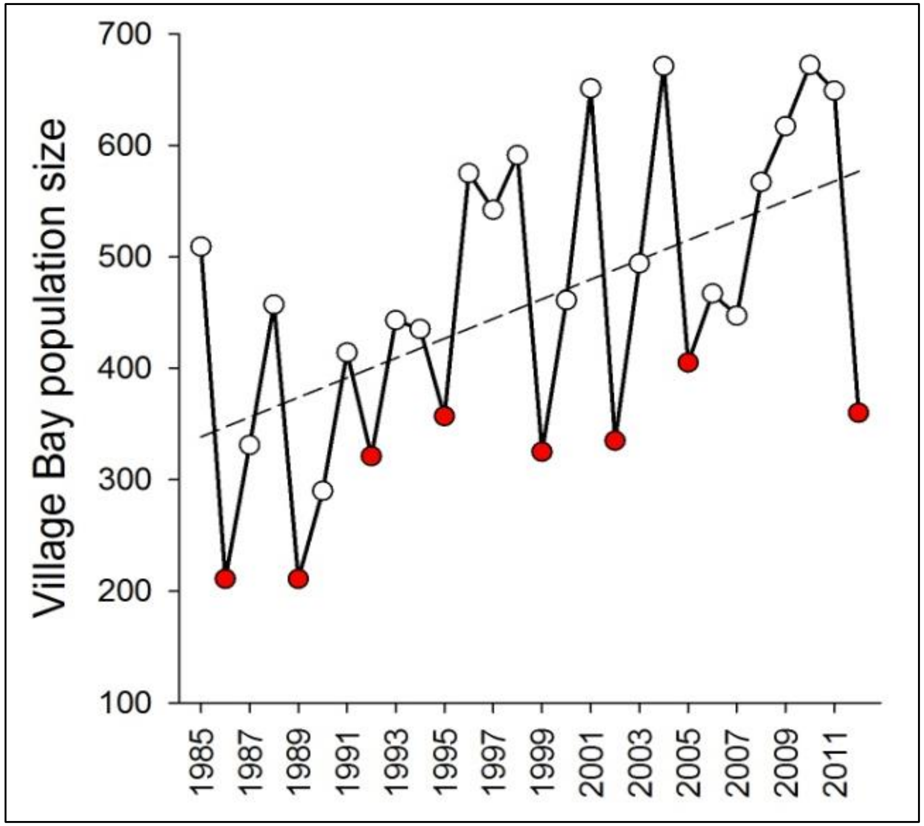
The Soay sheep population of Hirta, St. Kilda (Scotland)

Unmanaged population established in the 1930s from sheep introduced in the St Kilda archipelago about 4000 years ago

Population dynamics monitored since 1985
Individual marking, with ≈95% lambs caught within 1 week of birth

Pemberton and Clutton-Brock, 2004

Evolutionary ecology and dynamics of antibodies



- “Crashes” with up to 60% of the population dying during winter (≈ March)
- Population dynamics influenced by age and sex structure
- Roles of nutrition and parasites not fully explored, but potentially synergistic.

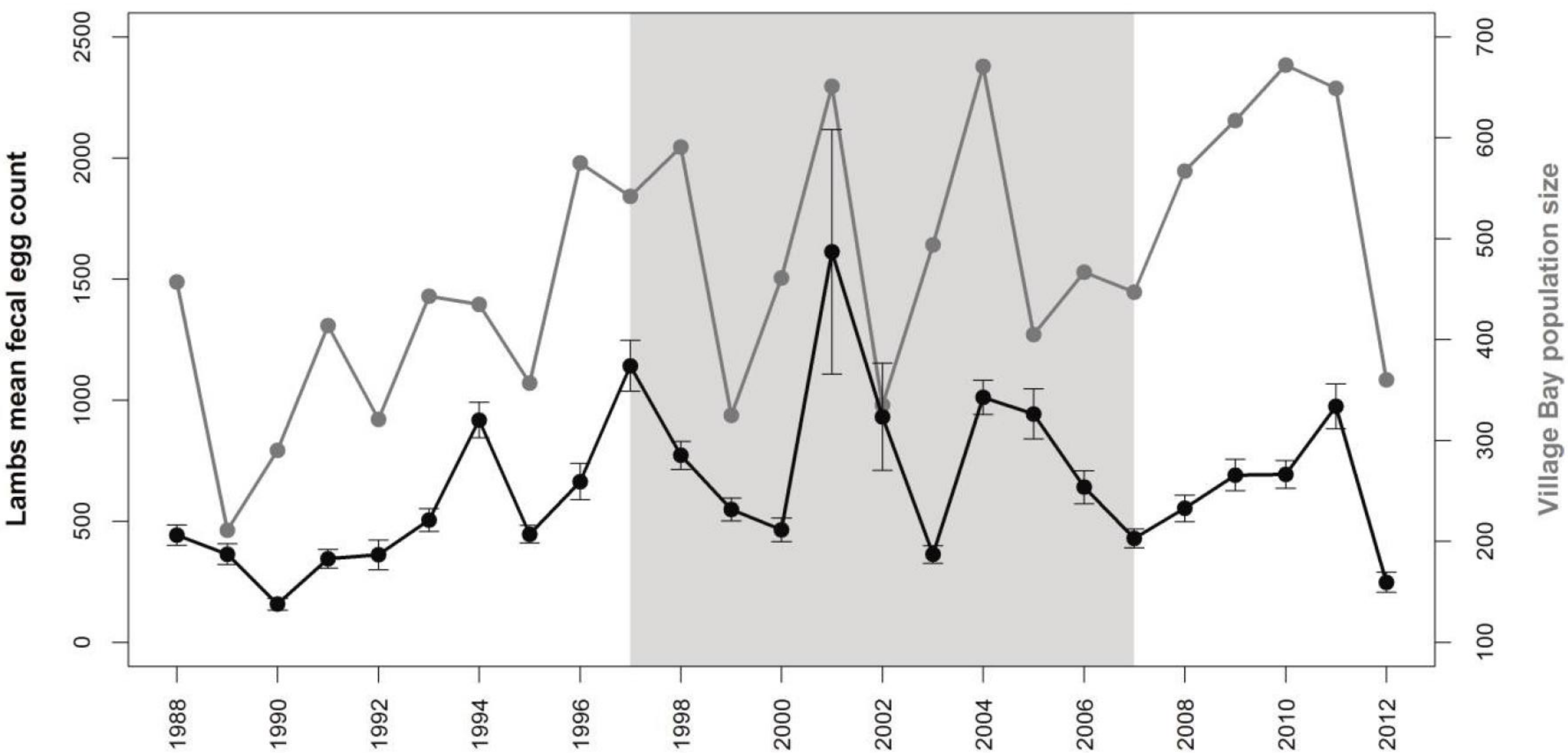
Gulland, Parasitology, 1992
Coulson et al., Science, 2001

Evolutionary ecology and dynamics of antibodies

Limited number of microparasites

Gastro-intestinal nematodes very important

- in young individuals



Hayward, Garnier et al., Am. Nat., 2014
Graham et al., Epidemiol. Infect., 2016

Evolutionary ecology and dynamics of antibodies

Limited number of microparasites

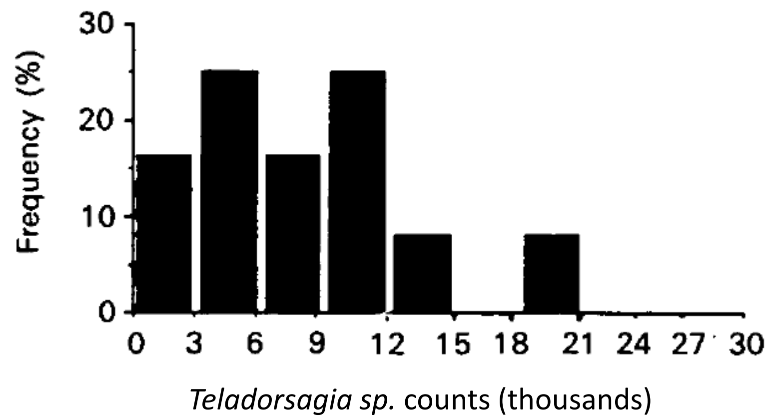
Gastro-intestinal nematodes very important

- in young individuals
- at the time of death during a crash

"The prevalance of gastrointestinal nematode infection in all age groups was 100%."

Table 3. The proportions of different gastrointestinal trichostrongyle species (mean ± s.e. % of total adults) found in lamb and adult Soay sheep on St Kilda in the 1989 population 'crash'

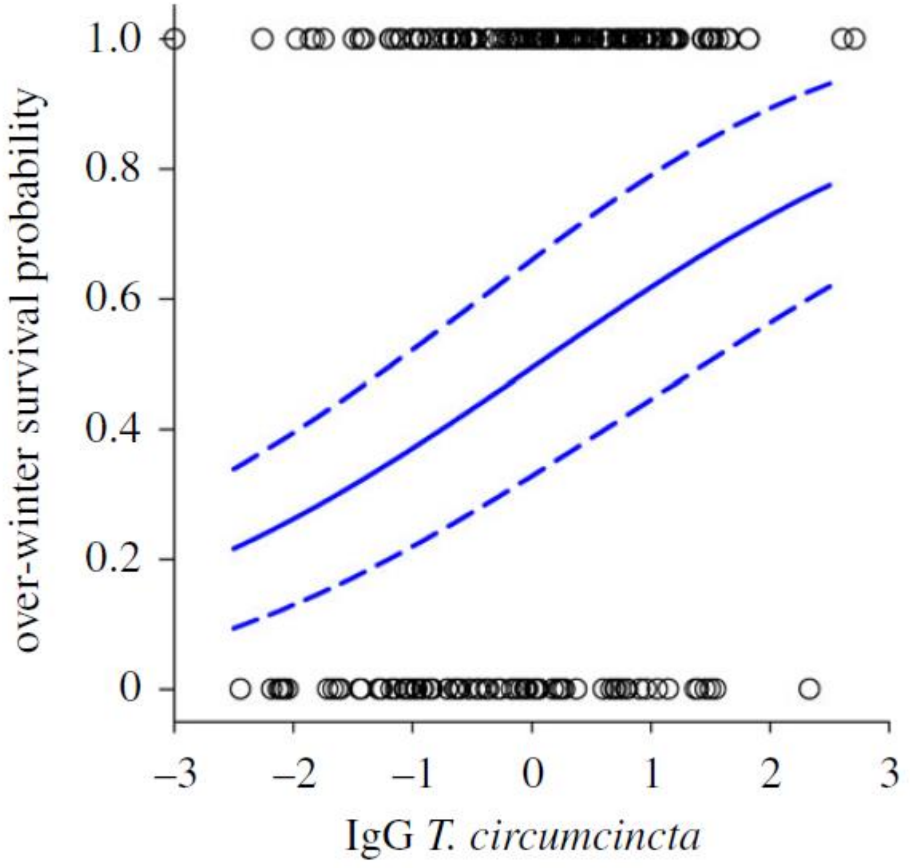
Species	Lambs ($n = 32$)	Adults ($n = 55$)
Ostertagia circumcincta, *Ostertagia trifurcata*, *Teladorsagia davtiani*	72 ± 12	78 ± 16
Trichonstrongylus axei	10 ± 8	11 ± 0
Trichonstrongylus vitrinus	13·2 ± 2	8 ± 1
Nematodirus battus, *Nematodirus filicollis*, *Nematodirus helvetianus*	1·8 ± 0·7	0·9 ± 0·6
Bunostomum trigonocephalum	0·45 ± 0·45	0·33 ± 0·3
Trichuris ovis	0·5 ± 0·3	0·18 ± 0·3
Chabertia ovina	2·3 ± 0·7	0·86 ± 0·2



Gulland, Parasitology, 1992

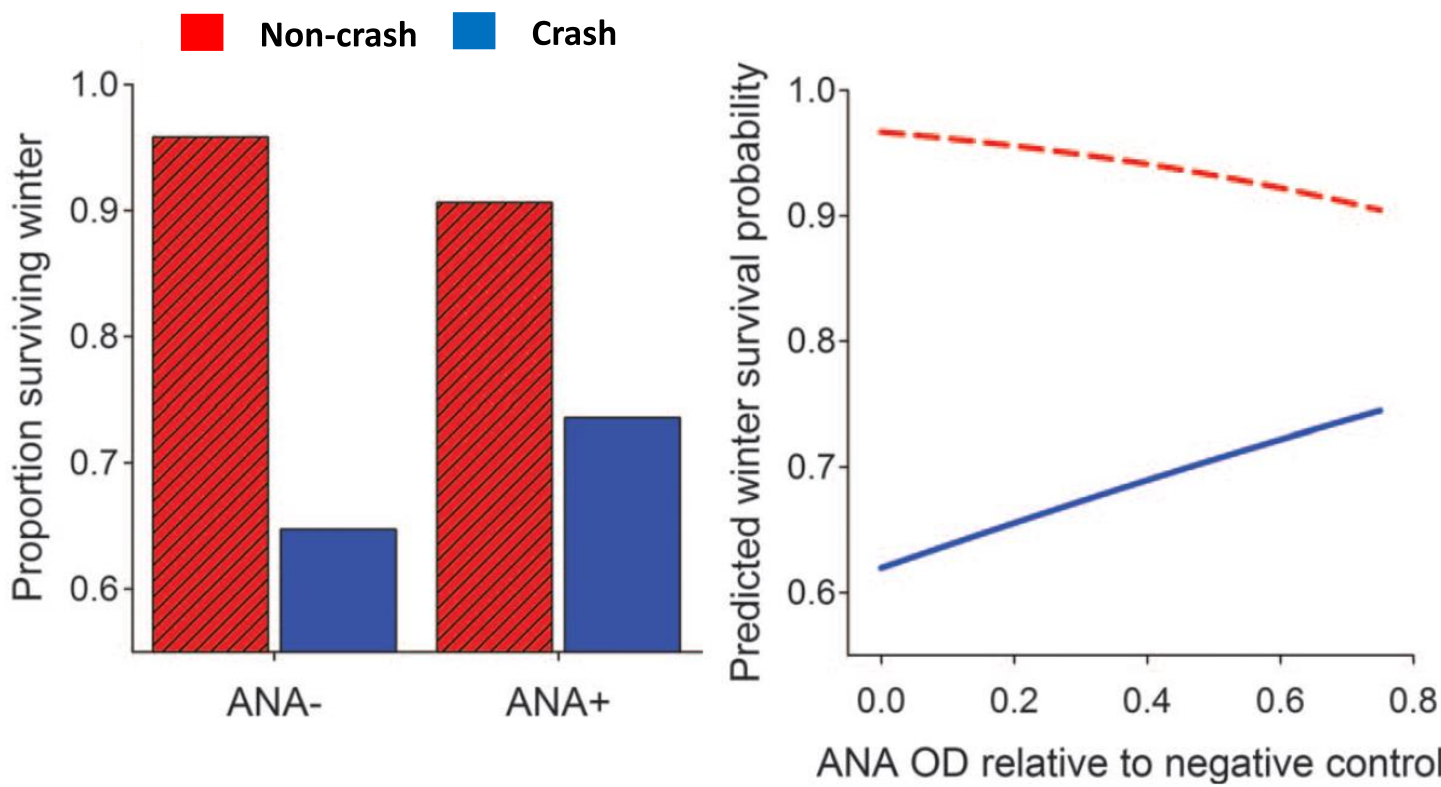
Evolutionary ecology and dynamics of antibodies

Association between anti-*T. circumcincta* immunoglobulin G and overwinter survival



Nussey et al., Proc. Roy. Soc. B, 2014

Anti-Nuclear Antibodies (ANA) over a period of 10 years - association between female winter survival and ANA levels in crash years only



Graham et al., Science, 2010

Evolutionary ecology and dynamics of antibodies

Only study of nutrition and pathology during the 1989 population crash

In individuals surviving the crash

Parameter	Season: Summer ($n = 27$)	P	Season: Crash ($n = 30$)
Total protein (g/l)	73·48 ± 2·78	****	64·86 ± 1·14
Albumin (g/l)	26·18 ± 1·48	****	22·62 ± 0·6
Albumin/globulin	0·42 ± 0·04	—	0·41 ± 0·02
Calcium (mmol/l)	2·55 ± 0·22	****	1·5 ± 0·09
Magnesium (mmol/l)	1·76 ± 0·61	—	1·03 ± 0·28
Phosphorus (mmol/l)	2·24 ± 0·2	****	1·43 ± 0·09
Urea (mmol/l)	5·73 ± 0·88	****	9·67 ± 0·37

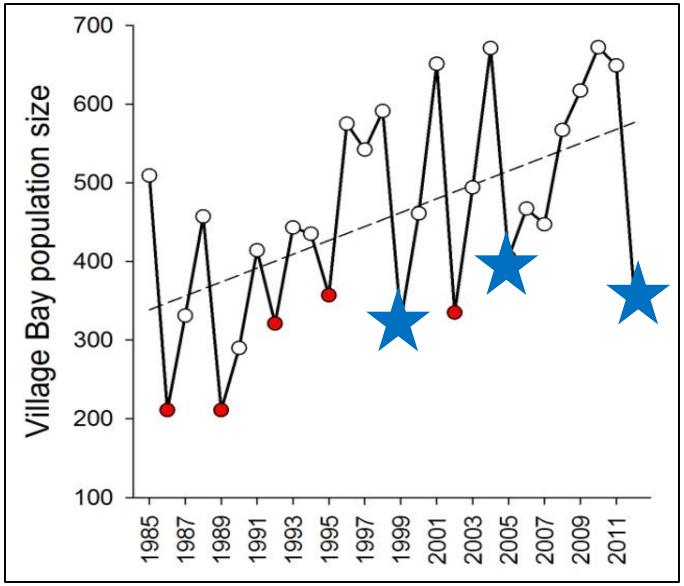
In dead individuals

"Carcasses were emaciated, with no subcutaneous, omental or perirenal fat"
"There was subcutaneous oedema, ascites, hydrothorax, hydropericardium"
"The liver was friable, with the typical 'nutmeg' appearance characteristic of passive congestion"

Malnutrition, especially proteins

Gulland, Parasitology, 1992

Evolutionary ecology and dynamics of antibodies



280 females over 2 years old caught in August prior to 3 population crashes

Age, Weight measured as part of core monitoring (important for overwinter survival, and fitness).

- **Nutritional markers:**
  - Albumin
  - Total proteins

  Colorimetric assay modified for low sample volumes
- **Antibody markers**
  - Anti-nuclear antibodies: modified human kit with sheep secondary antibody
  - Anti-*T. circumcincta* immunoglobulin G

Garnier et al., Ecology Letters, 2017

Evolutionary ecology and dynamics of antibodies

Impossible to select a best model for overwinter survival using these markers

- Set of best models includes effects of IgG and various combinations of the three other predictors

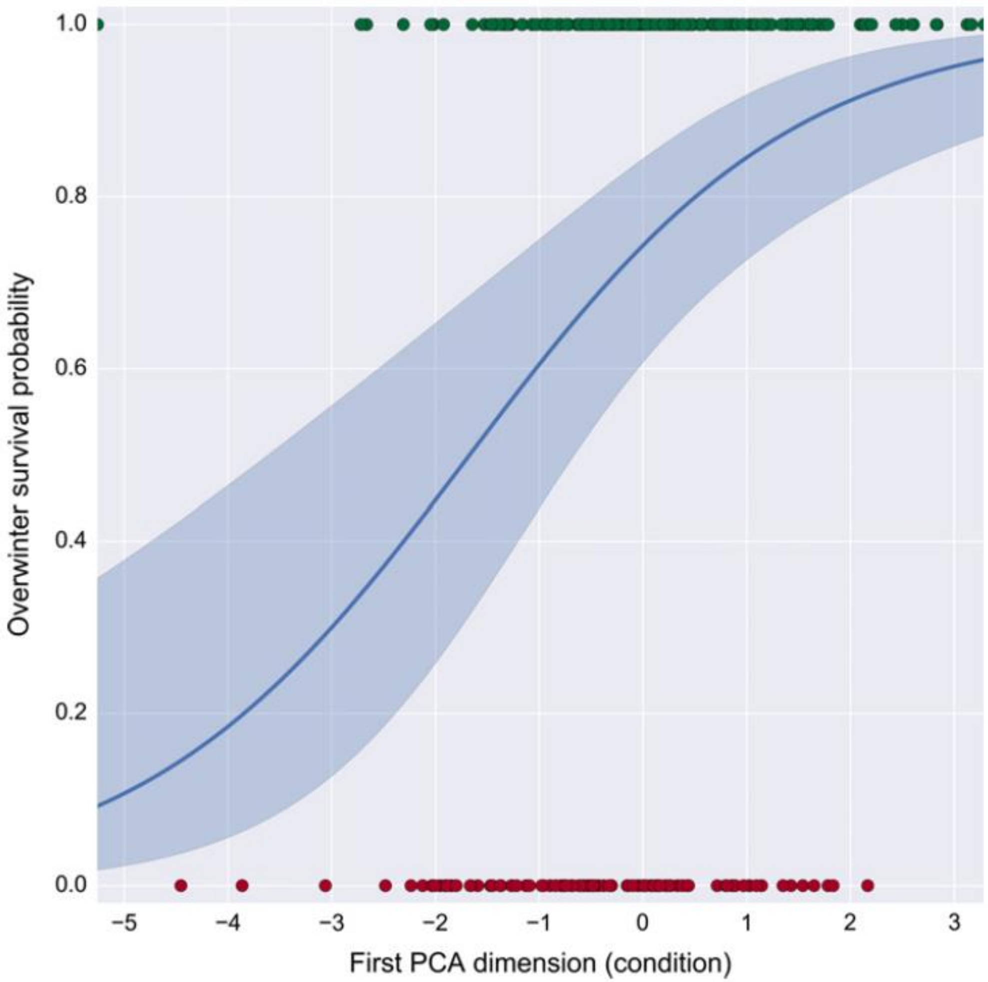
Complex correlation structure between the markers

Use a PCA to better parse the joint as well as distinct effects of nutrition and immunoglobulins.

Garnier et al., Ecology Letters, 2017

Principal component analysis – Survival correlates

- Significant positive association between the first PCA dimension and survival



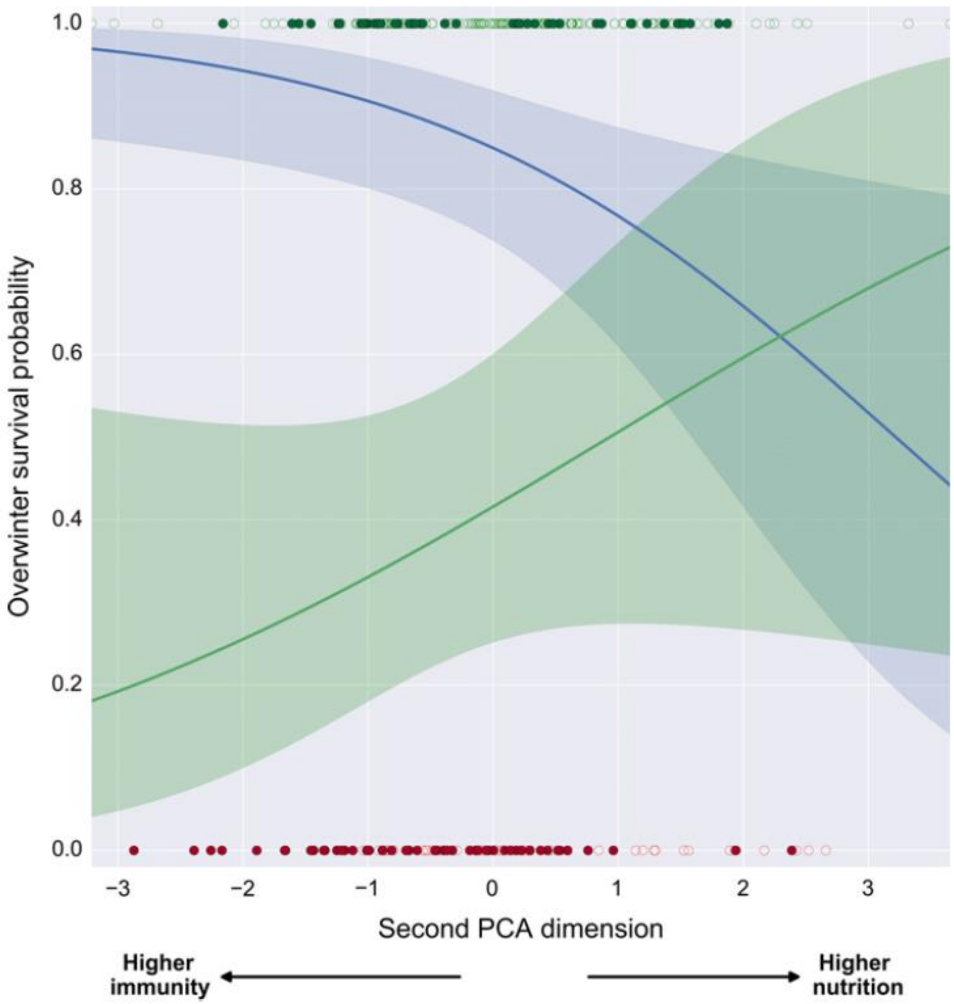
➡ In accordance with PC1 being a marker of condition

Garnier et al., Ecology Letters, 2017

Evolutionary ecology and dynamics of antibodies

Principal component analysis – Survival correlates

- Significant positive interaction between the age class and the PCA second dimension (p=0.004).



Older females ➡ Investment in nutrition > immunity

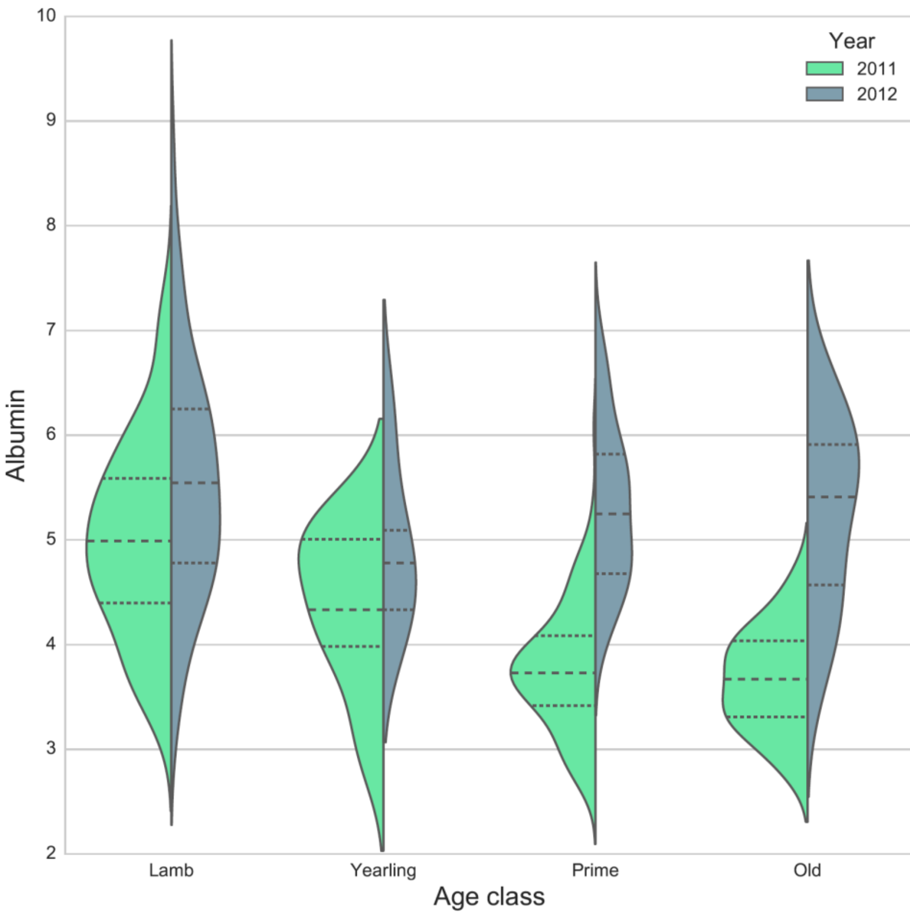
Primeage females ➡ Investment in immunity > nutrition

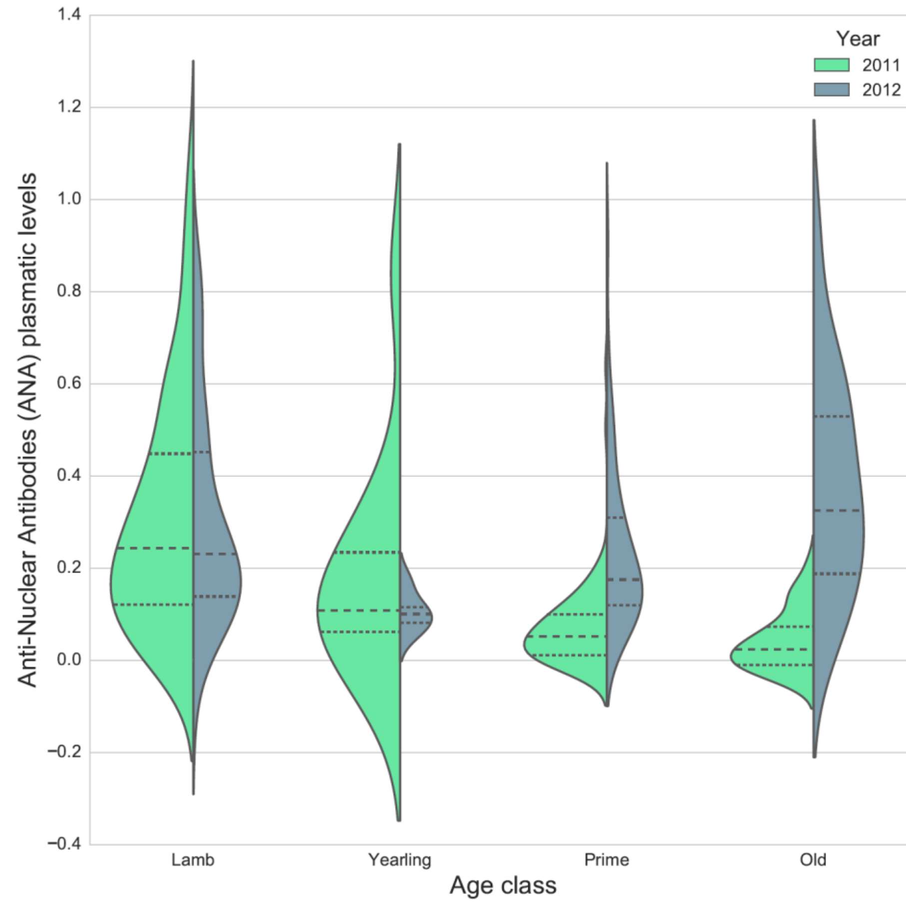
Garnier et al., Ecology Letters, 2017

Evolutionary ecology and dynamics of antibodies

Markers rebound after a population crash – accurate currencies

Differences between age classes – females paying a nutritional cost in pre-crash years





Garnier et al., Sci Nat, 2017

Evolutionary ecology and dynamics of antibodies

Identification of a novel condition marker, independent of weight and frame size, associated with individual fitness

Rare evidence for a trade-off between investment in immunity and homeostasis, with age-dependent fitness effects

- Use PC2 as a point estimate of tolerance in a resistance/tolerance context?

Some support for the occurrence of a negative spiral involving nematodes, malnutrition and immunity in the Soay sheep.

- Histopathology likely to provide further insights

Caudron, Garnier et al. ,Roy Soc Open Science, 2017

Interest in getting a nutritional time series for proteins and in measuring markers of fat metabolism

- Use possible serum biobanks to extend this approach to other ungulates (caribou/reindeer, moose, elk…)

Epidemiology and dynamics of antibodies

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Epidemiology and dynamics of antibodies

Bats are important reservoirs of potentially zoonotic viruses (Hendra, Nipah, SARS, MERS, Marburg, Ebola…)

But little is known of the dynamics of their immunity to viruses

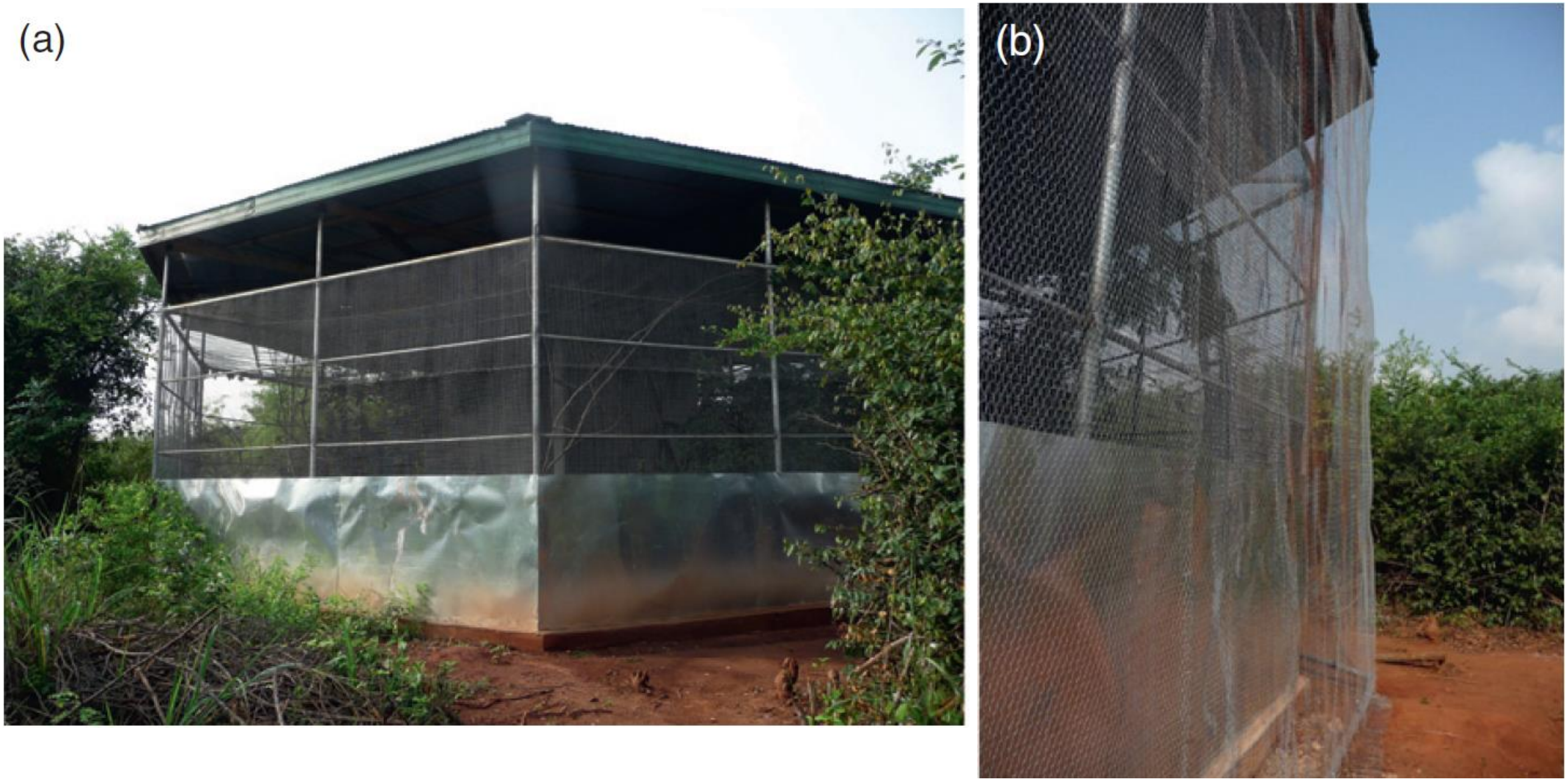
Crucial to parameterize epidemiological models in wild bat populations

Low recapture rates of wild bats (particularly tree-dwelling) make it difficult to obtain individual antibody dynamics

Use a captive colony of reproducing African straw-coloured fruit bats, naturally infected with African henipaviruses

(but seemingly devoid of filoviruses and rabies!!)

Epidemiology and dynamics of antibodies



Hexagonal structure 27·5 m in diameter and 3·5 m in height.

Colony established in 2009, with 3 cohorts totaling 77 individuals captured in Accra
Population variable, 100 - 125 individuals
Second facility with smaller cages for isolation (and experimental infection)

Epidemiology and dynamics of antibodies

Early studies:

- Possible **seasonal dynamics** of anti-henipaviruses in females
- Existence of a transfer of anti-henipaviruses of antibodies

Baker et al., Journal of Animal Ecology, 2014

Ideal setting to study long term persistence of viruses in bat populations

- Low level persistence vs recrudescence?
- >1500 samples / >300 individuals between 2009 and 2016 with measured anti-henipavirus antibodies

Epidemiology and dynamics of antibodies

Henipavirus antibody lelvel

Date

Some individuals keep anti-henipaviruses antibodies over several years

Recurrent boosting of immunity may indicate that the virus(es) is/are still circulating in the captive colony

Upcoming analysis using capture-recapture models to estimate seroconversion and seroreversion rates

Epidemiology and dynamics of antibodies

Antibody dynamics have the potential to be used in a wide range of questions in ecology, evolution and epidemiology

Still plenty of untapped potential in wild animal populations, especially with the development of -omics

Immune response after Ebola / Nipah vaccination in 2 species of fruit bats by transcriptomics

Data collection ongoing

Long term study of Indian yellow-nosed albatrosses exposed to avian cholera

Centre d'Ecologie Fonctionnelle & Evolutive

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