

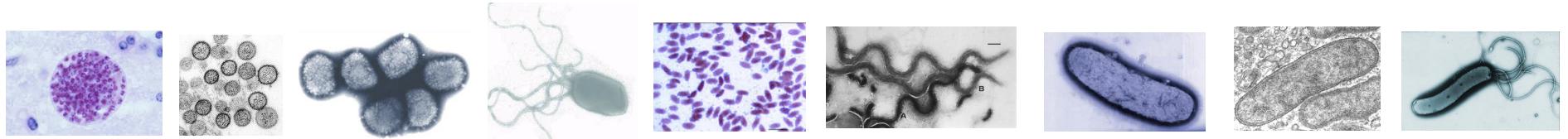
Pathobiome diversity and co-infection patterns in a community of rodents

Jessica Abbate, Maxime Galan, Yannick Chaval, Cécile Gotteland, Maria Razzauti, Tarja Sironen, Liina Voutilainen, Heikki Henttonen, Patrick Gasqui, Jean-François Cosson, Nathalie Charbonnel



Pathobiome Paris, June 24, 2015
jessie.abbate@gmail.com

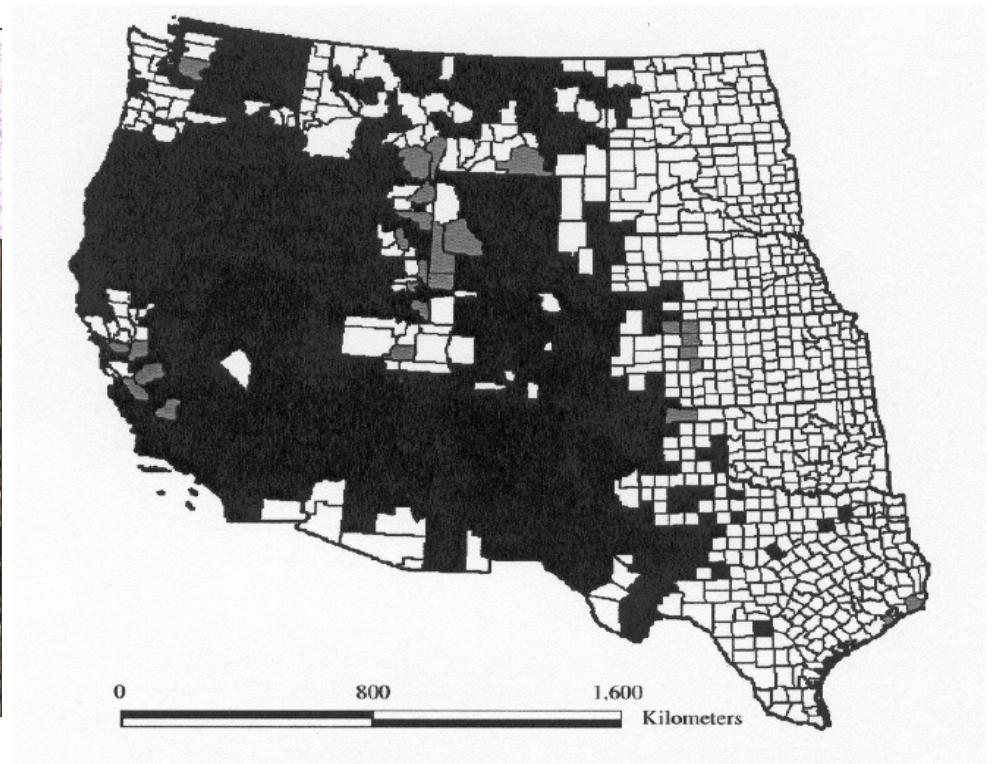
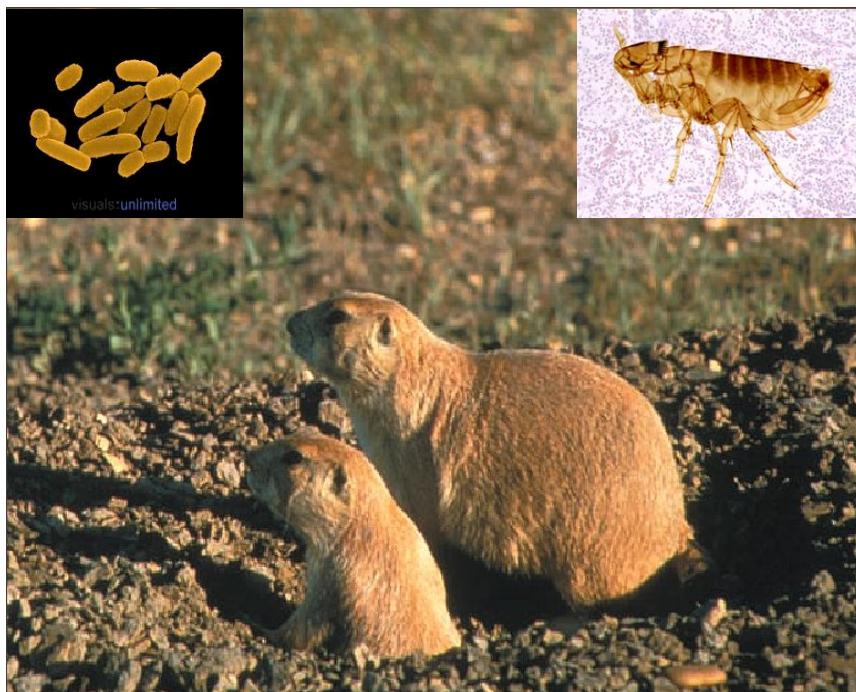




Background



DETERMINANTS of DISEASE DISTRIBUTION in NATURE

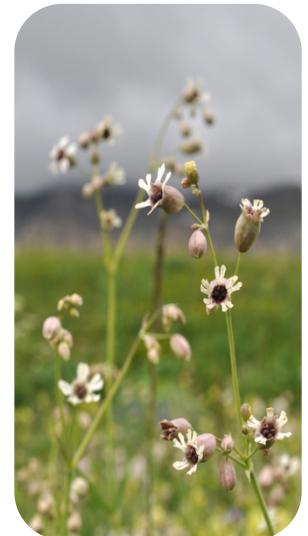
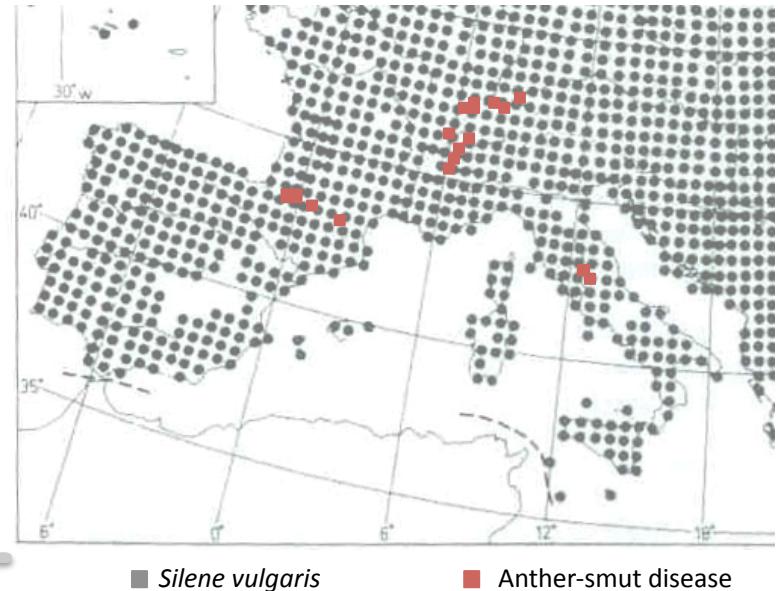
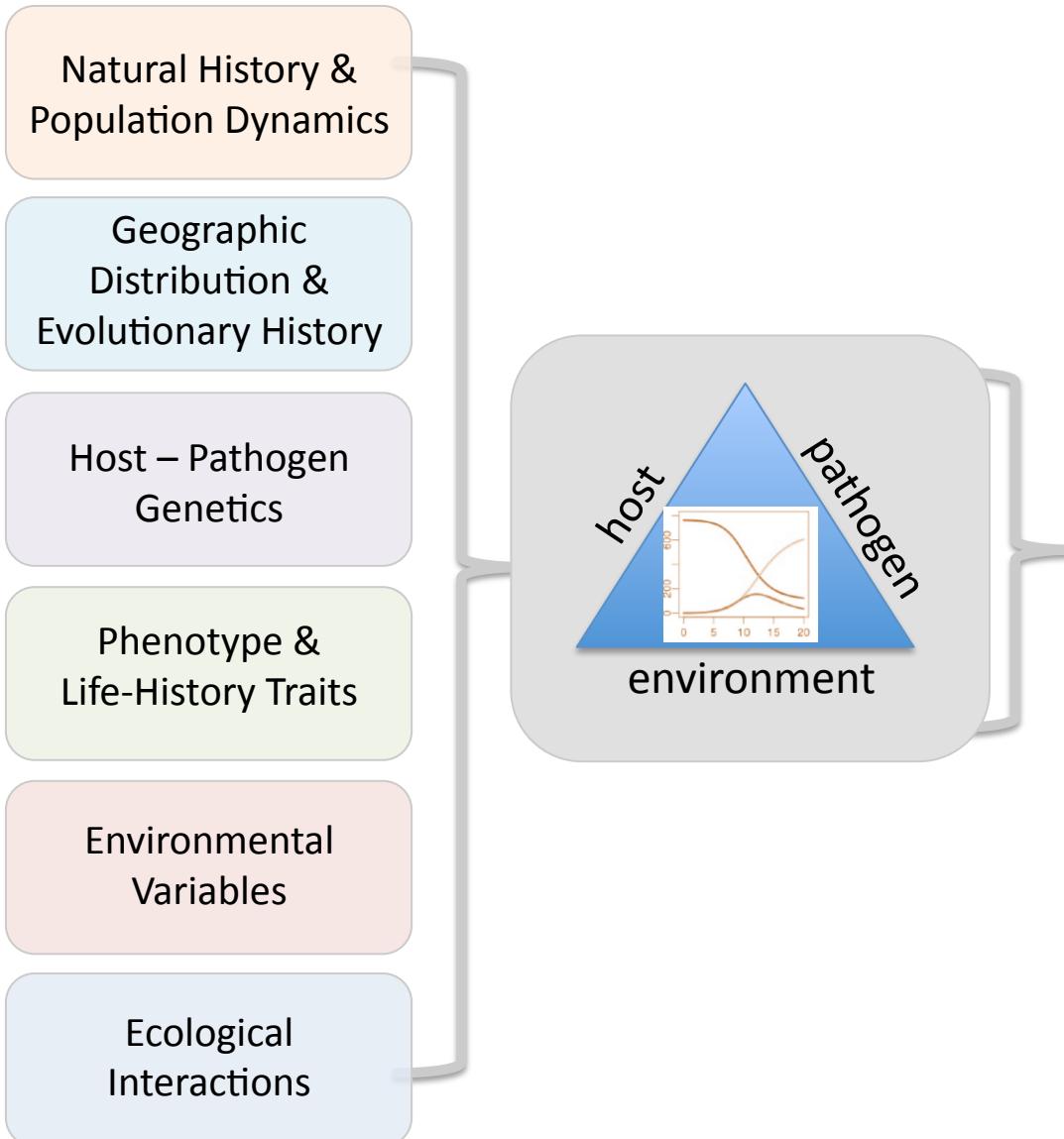


Example:

Sylvatic Plague in small mammals limited to
west of the 100th Meridian

Antolin et al. 2002; Strapp et al. 2004

DETERMINANTS of DISEASE DISTRIBUTION in NATURE



Abbate & Antonovics 2014 *Oikos*

DETERMINANTS of DISEASE DISTRIBUTION in NATURE

Natural History & Population Dynamics

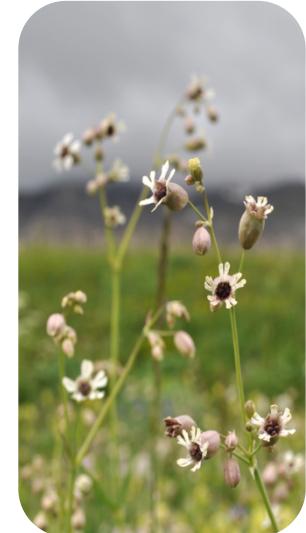
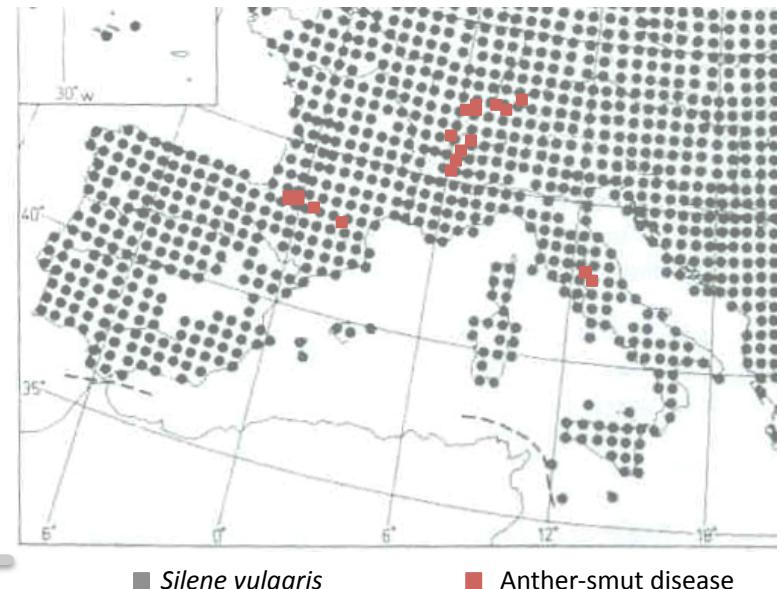
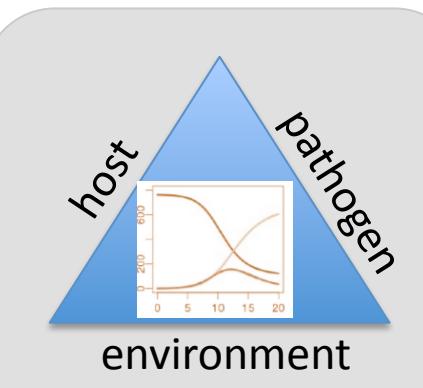
Geographic Distribution & Evolutionary History

Host – Pathogen Genetics

Phenotype & Life-History Traits

Environmental Variables

Ecological Interactions



Abbate & Antonovics 2014 *Oikos*

DETERMINANTS of DISEASE DISTRIBUTION in NATURE

Natural History & Population Dynamics

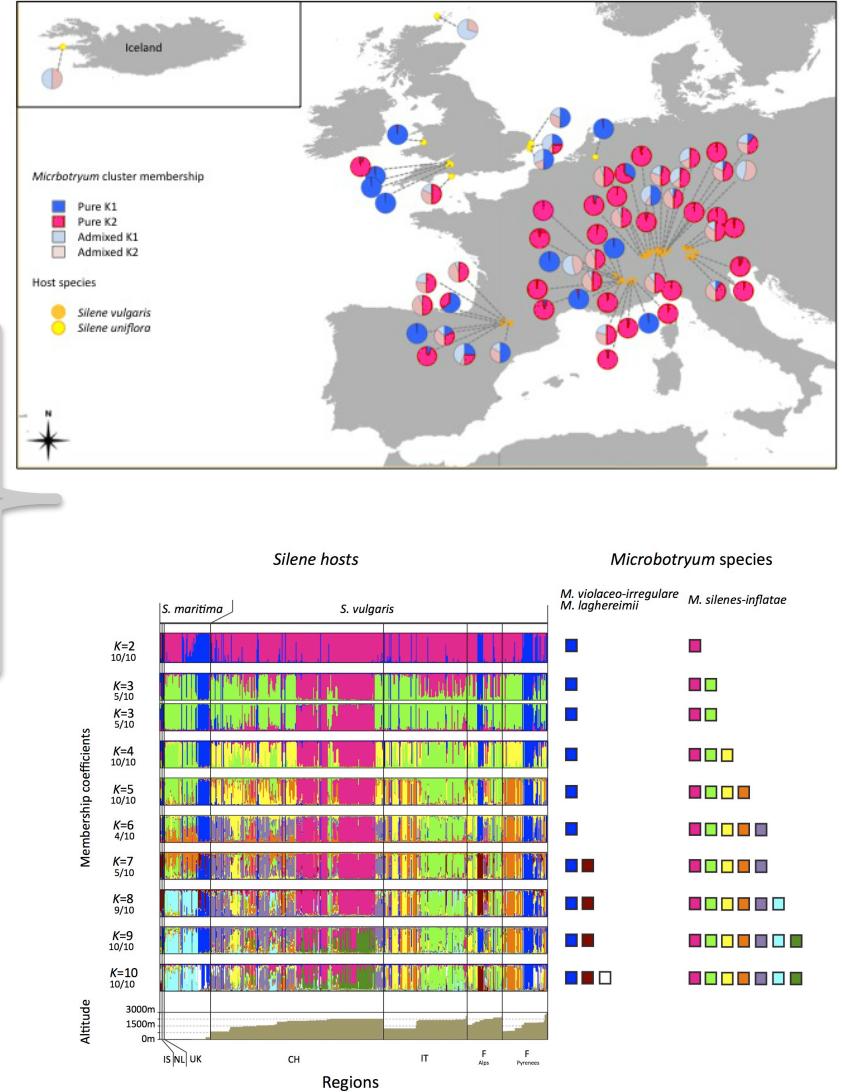
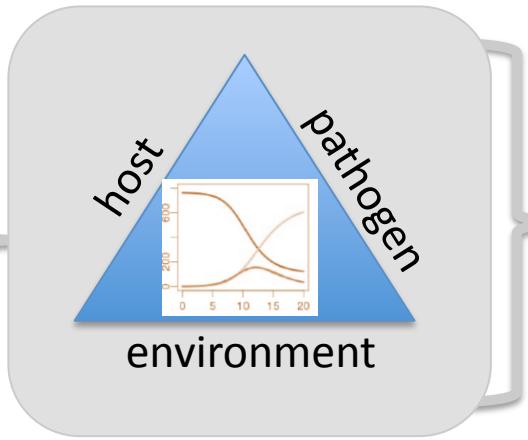
Geographic Distribution & Evolutionary History

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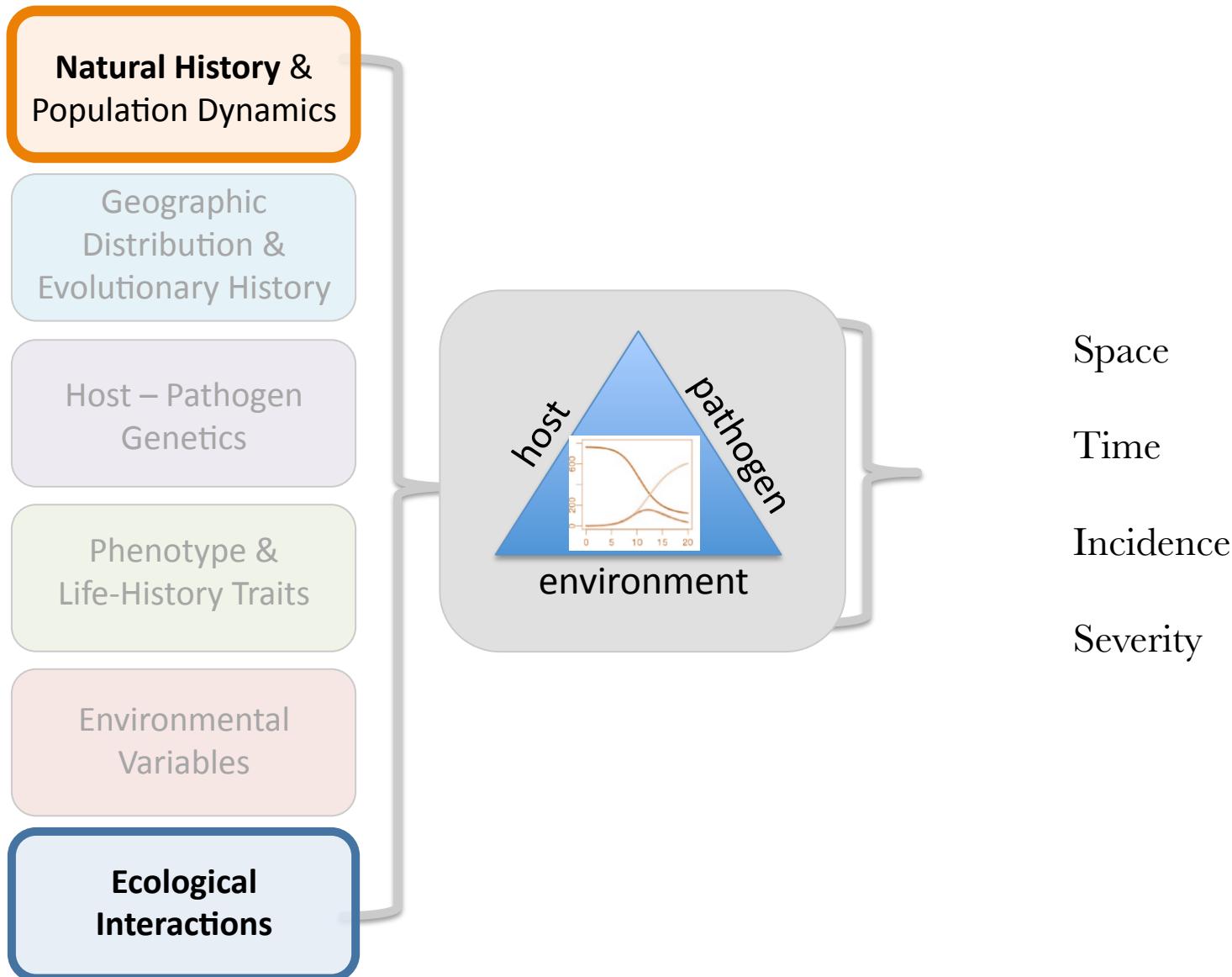
Environmental Variables

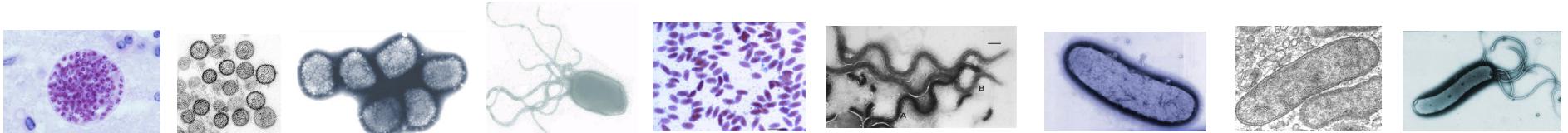
Ecological Interactions



Gladieux, Abbate, Giraud, et al. *in prep*

DETERMINANTS of DISEASE DISTRIBUTION in NATURE





The study

Pathobiome diversity and co-infection patterns in a community of rodents



Natural History &
Population Dynamics

Geographic
Distribution &
Evolutionary History

Host – Pathogen
Genetics

Phenotype &
Life-History Traits

Environmental
Variables

Ecological
Interactions

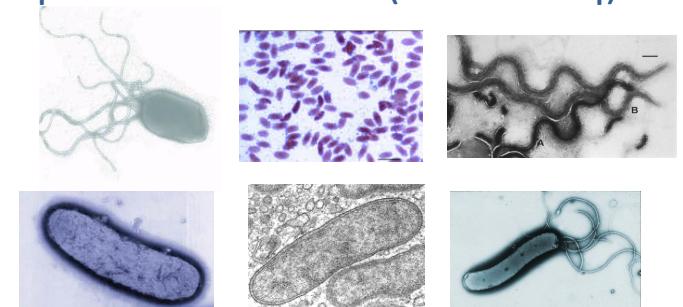
Pathobiome diversity (natural history)

&

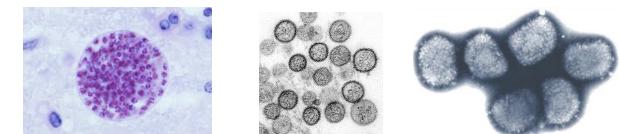
Rodent blood infections



- Splenic microbiota (16S MiSeq)



- Viral and protazoan seropositivity



- Nematodes & Ectoparasites

co-infection patterns

Natural History & Population Dynamics

Geographic Distribution & Evolutionary History

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Ecological Interactions

Cricetidae



Microtus agrestis
(field vole)



Microtus arvalis
(common vole)



Microtus subterraneus
(European pine vole,
Common pine vole)



Myodes glareolus
(bank vole)

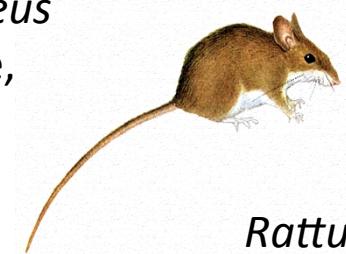


Arvicola scherman
(Montane water vole)

Muridae



Apodemus sylvaticus
(wood mouse)



Apodemus flaviculus
(yellow tailed
mouse)



Rattus norvegicus
(brown rat)

Natural History & Population Dynamics

Geographic Distribution & Evolutionary History

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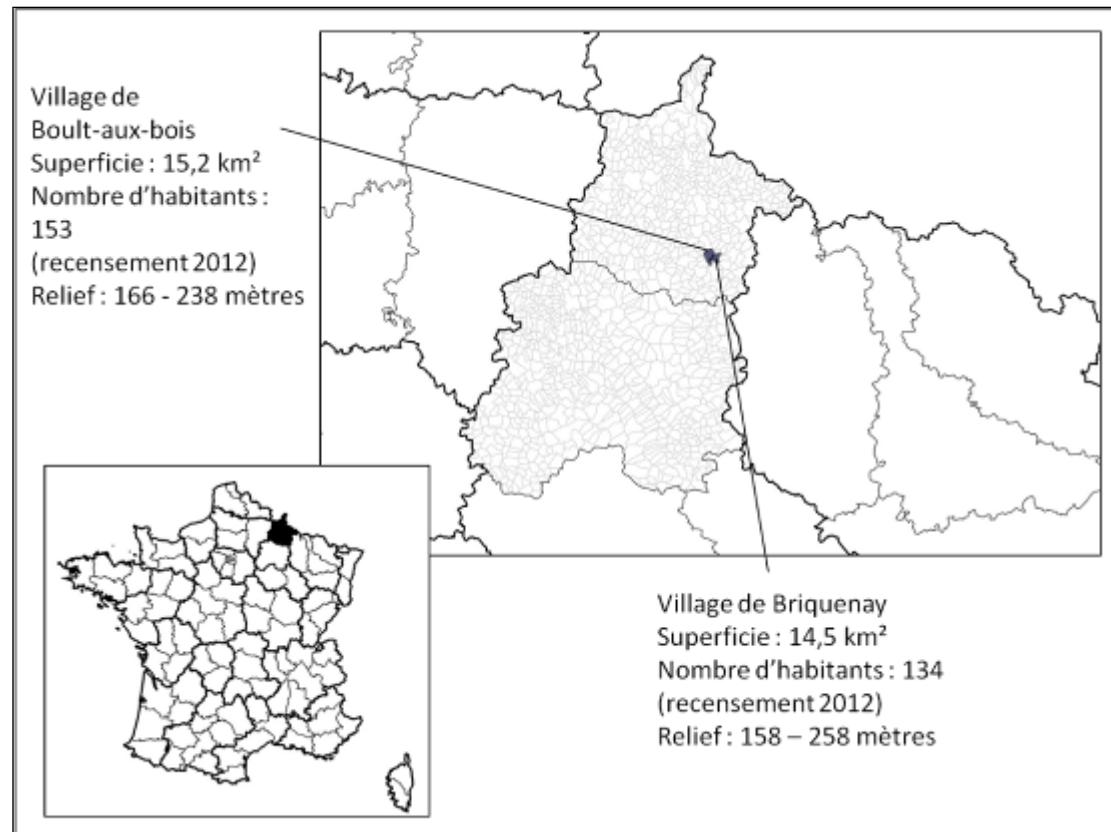


Figure 7 : Localisation et identité des deux sites d'études

Natural History & Population Dynamics

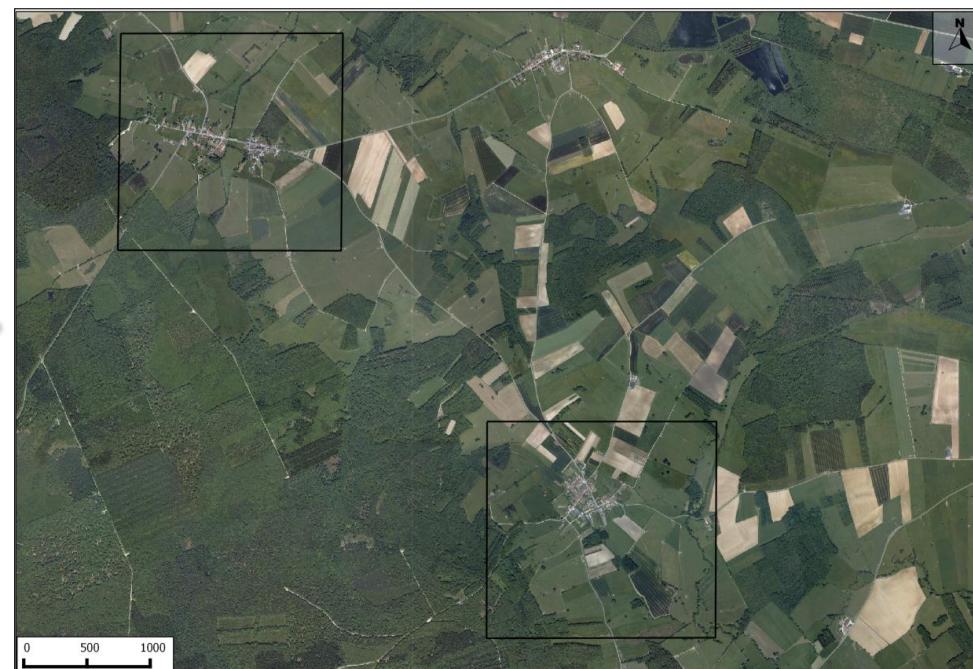
Geographic Distribution & Evolutionary History

Host – Pathogen Genetics

Phenotype & Life-History Traits

Environmental Variables

Ecological Interactions



Forestiers



Prairiaux



Anthropisés



Natural History & Population Dynamics

Geographic Distribution & Evolutionary History

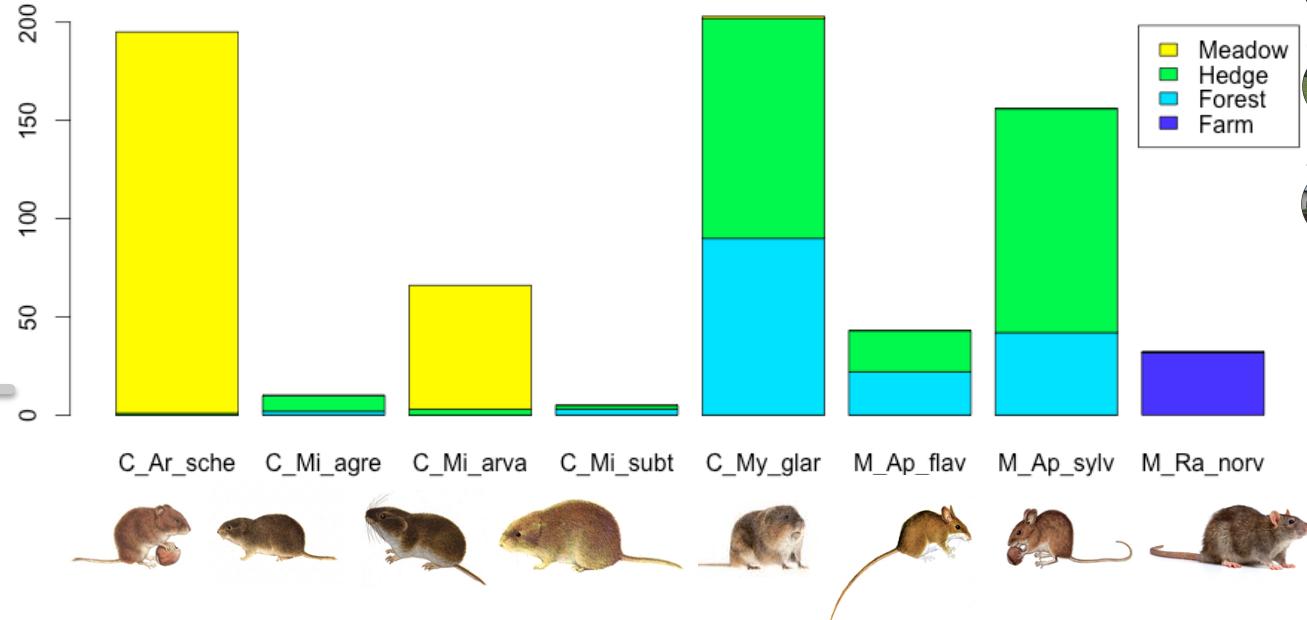
Host – Pathogen Genetics

Phenotype & Life-History Traits

Environmental Variables

Ecological Interactions

N=710



Natural History & Population Dynamics

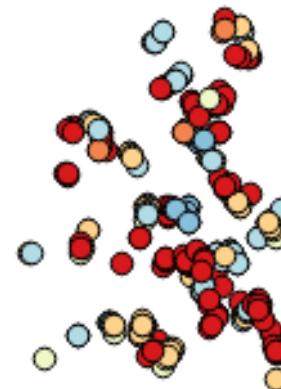
Geographic Distribution & Evolutionary History

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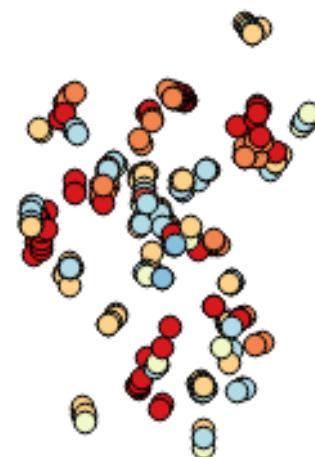
Environmental Variables

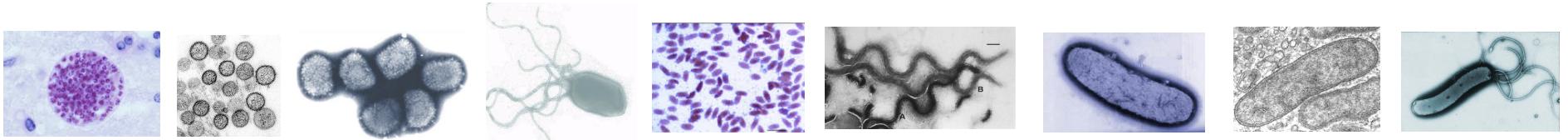
Ecological Interactions



hosts

- C_Ar_sche
- C_Mi_agre
- C_Mi_arva
- C_Mi_subt
- C_My_glar
- M_Ap_flav
- M_Ap_sylv
- M_Ra_norv





Pathobiome Diversity (natural history)



Pathobiome diversity (natural history)

Natural History &
Population Dynamics

Geographic
Distribution &
Evolutionary History

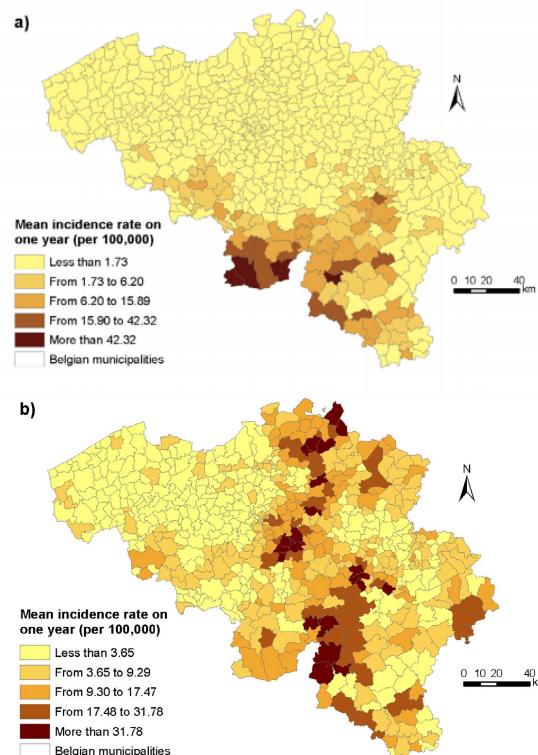
Host – Pathogen
Genetics

Phenotype &
Life-History Traits

Environmental
Variables

Ecological
Interactions

Determinants of the geographic distribution of Puumala virus and Lyme borreliosis infections in Belgium



Linard et al. 2007 *Int J Health Geographics*

Pathobiome diversity (natural history)

Natural History &
Population Dynamics

Geographic
Distribution &
Evolutionary History

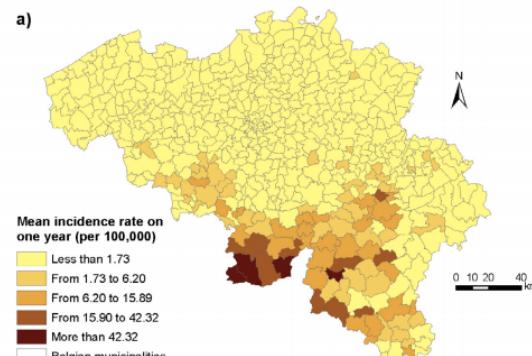
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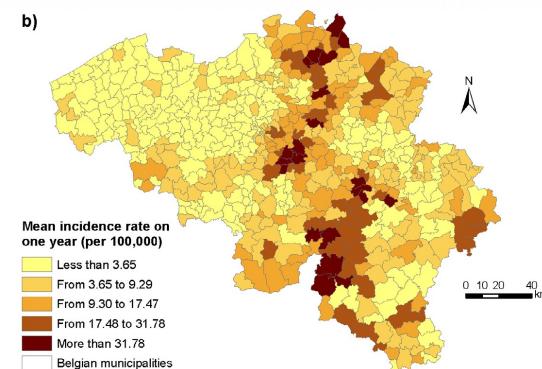
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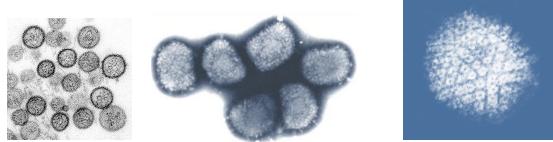


Myodes glareolus
(bank vole)



Ixodes ricinus

Linard et al. 2007 *Int J Health Geographics*



Viruses (N=675)

- Cowpox Virus (OPXV)

32.9% prev.

- Hantaviruses

(PUUV, TULV)

2.4% prev.

- Lymphocytic Choriomeningitis Virus

(LCMV)

3.2% (2/62) *M. arvalis*

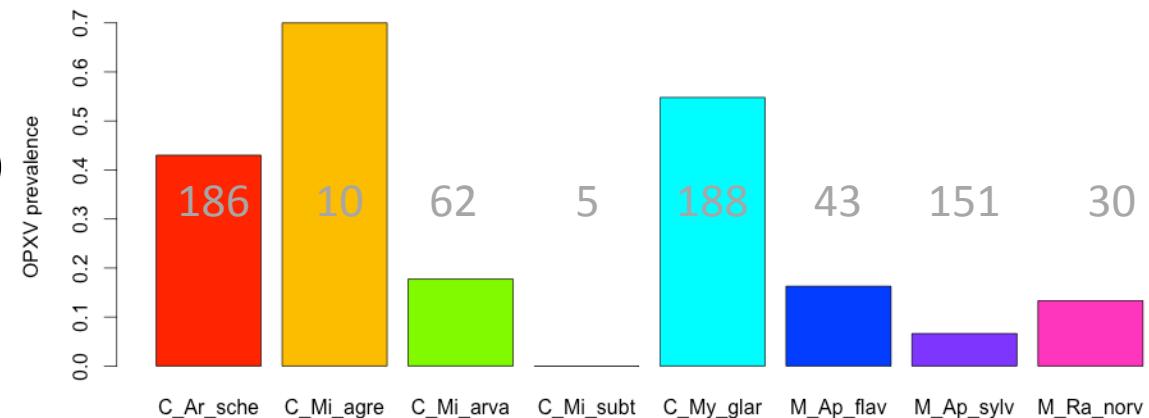




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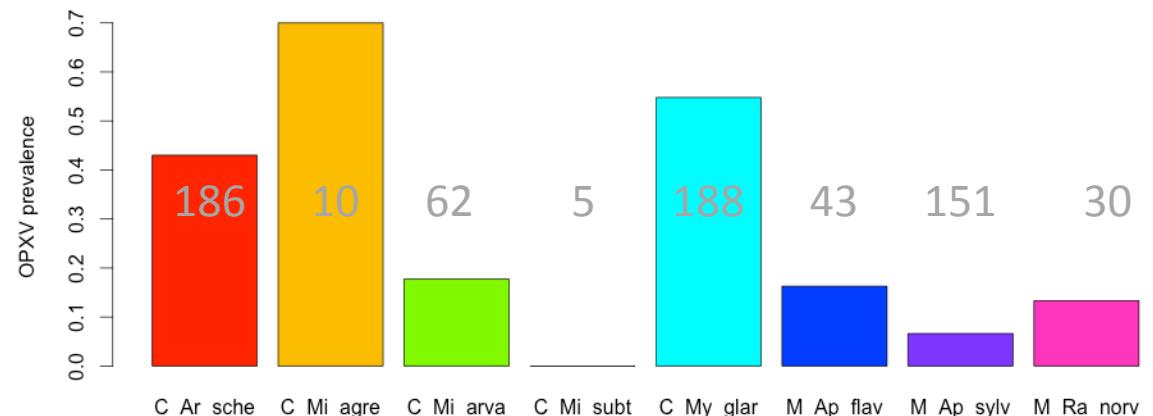




Viruses (N=675)

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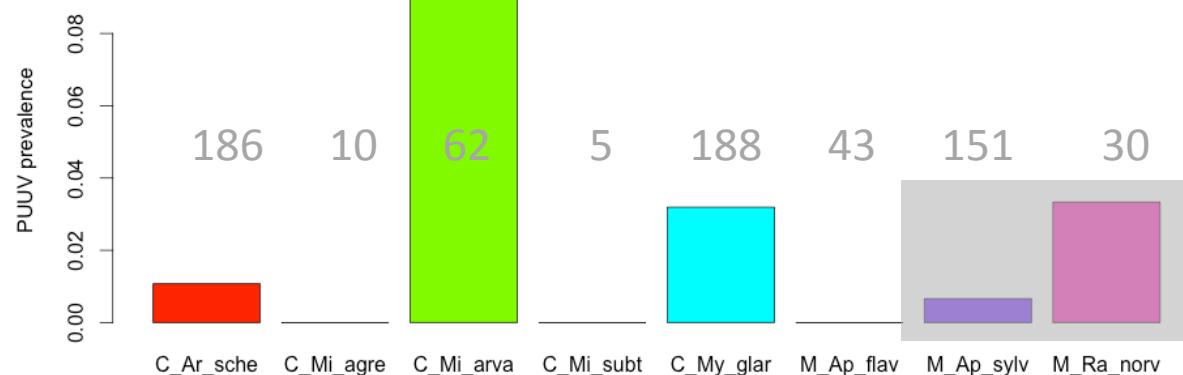
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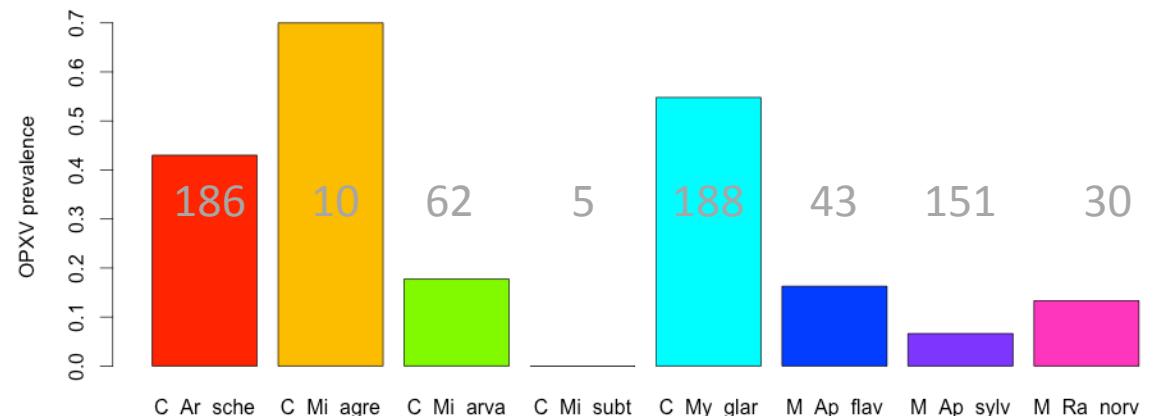




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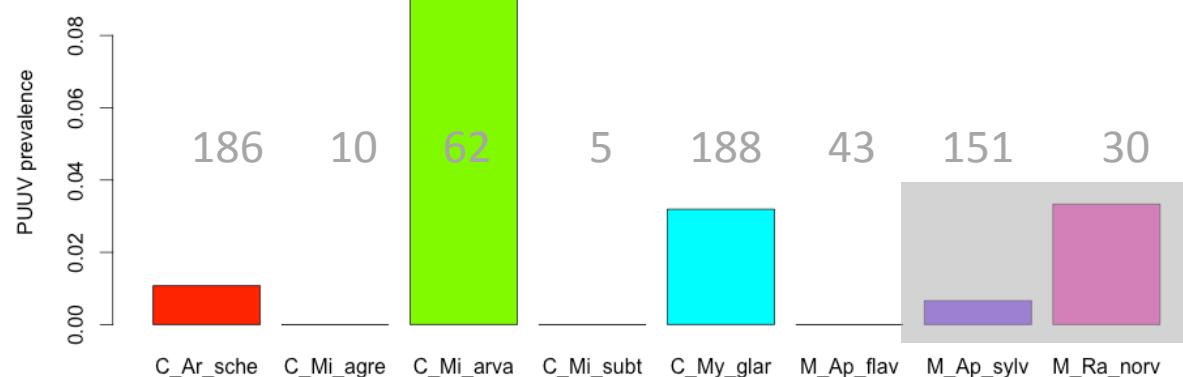
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- Hantaviruses

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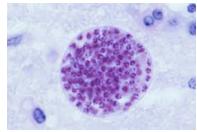
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Protazoa(n)

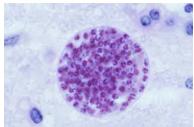
- *Toxoplasma gondii* antibodies (N=685)

7.2% prev.

- *Toxoplasma* or other eukaryotic (*Coccidian*) undefined OTU (N=315)
(16S - MiSeq)

4.1% prev.

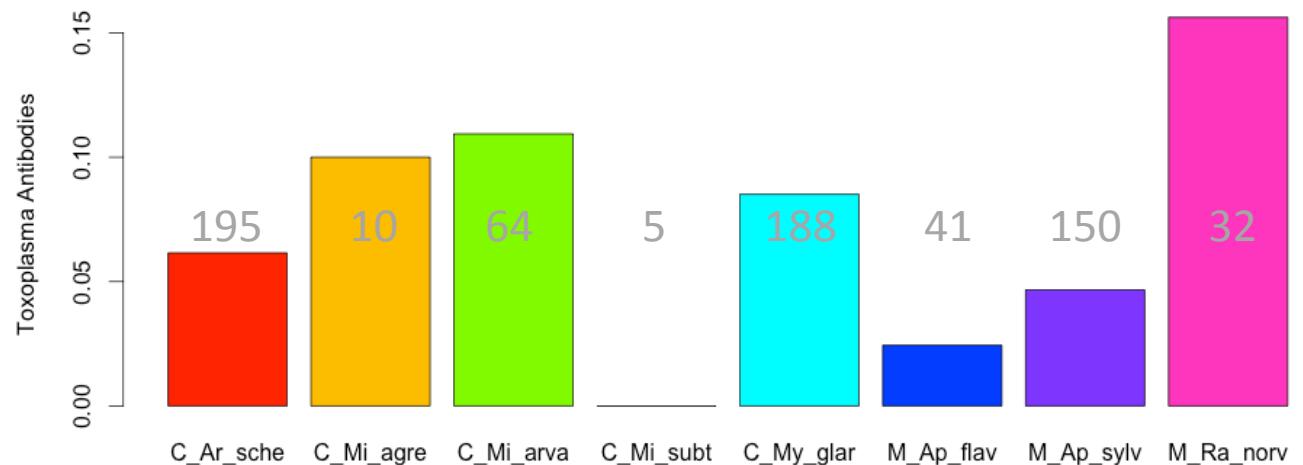




Protazoa(n)

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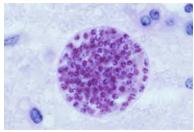
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Protazoa(n)

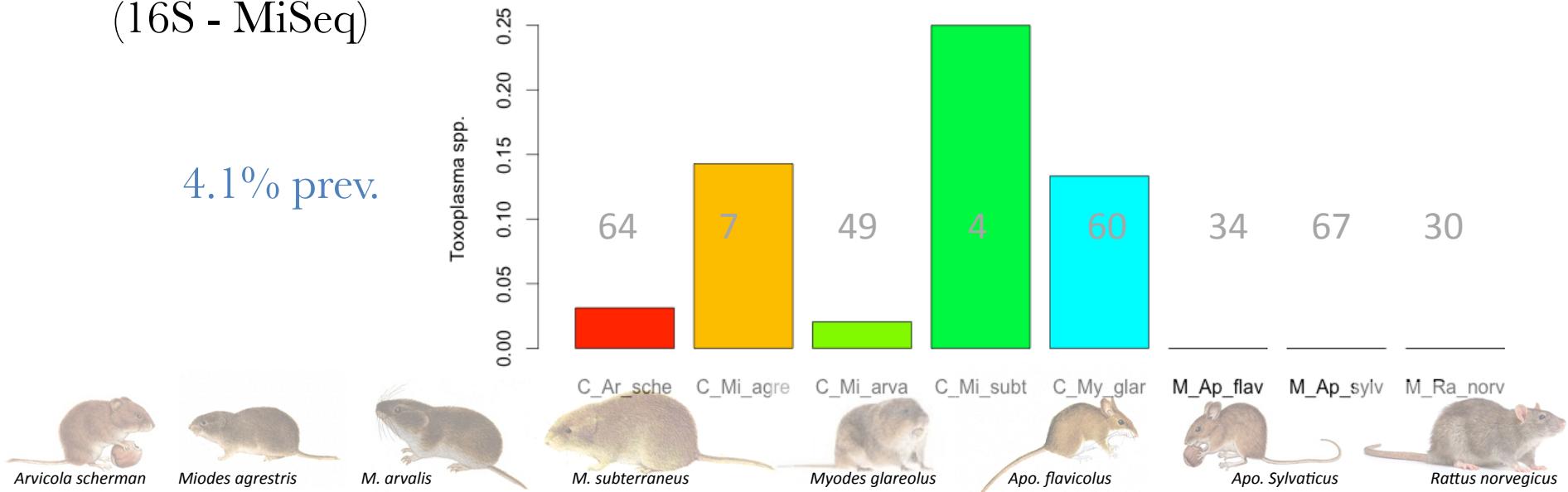
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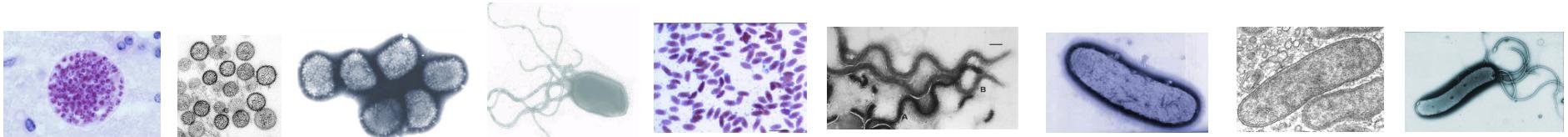
7.2% prev.



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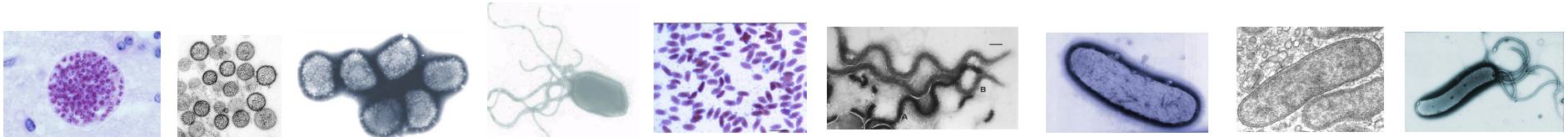


Bacteria MiSeq (N=315)

- 954 OTUs >50 reads ; 591 prev > 0
- 184 OTUs >500 reads ; 146 with prev >0
- 31 pathogenic OTUs (15 species minimum)

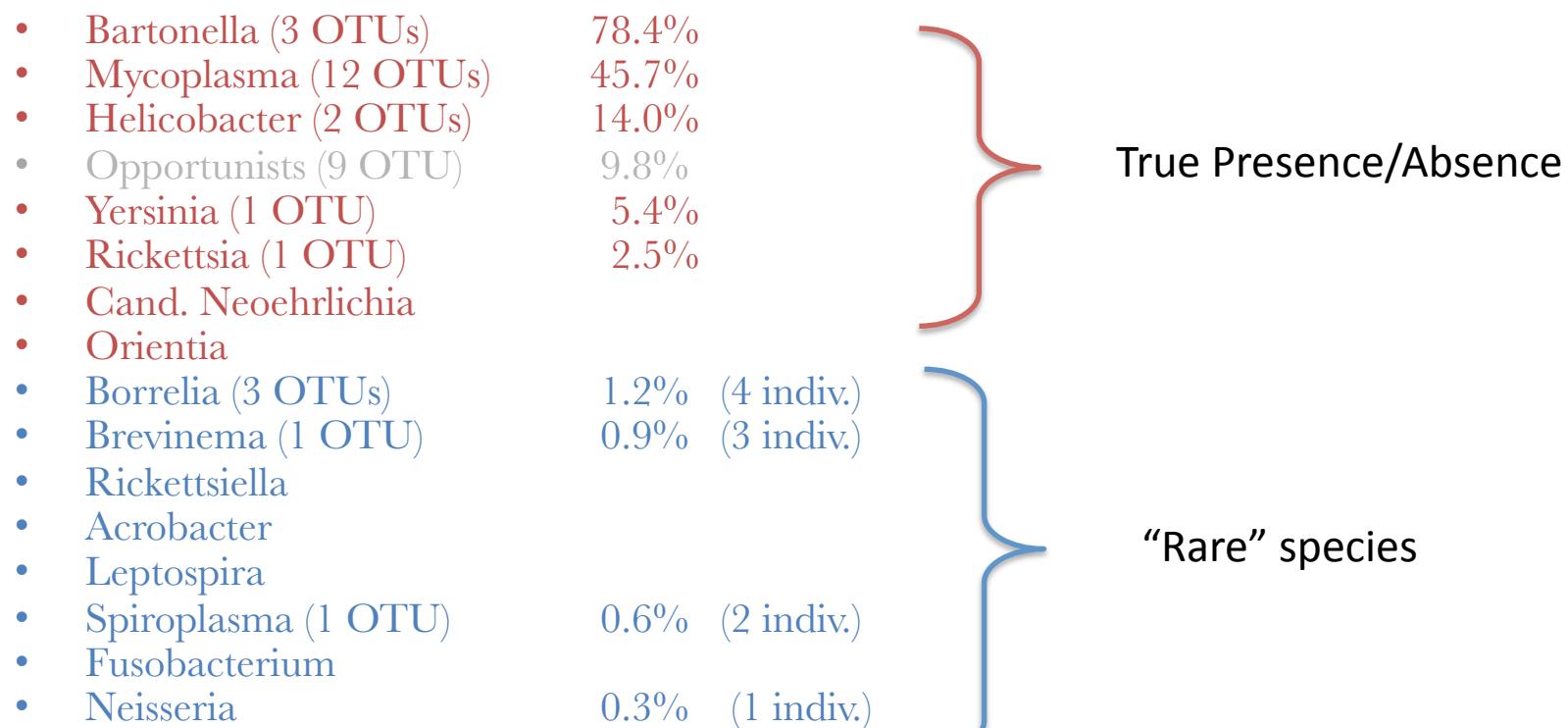
• Bartonella (3 OTUs)	78.4%
• Mycoplasma (12 OTUs)	45.7%
• Helicobacter (2 OTUs)	14.0%
• Opportunists (9 OTU)	9.8%
• Yersinia (1 OTU)	5.4%
• Rickettsia (1 OTU)	2.5%
• Cand. Neoehrlichia	
• Orientia	
• Borrelia (3 OTUs)	1.2% (4 indiv.)
• Brevinema (1 OTU)	0.9% (3 indiv.)
• Rickettsiella	
• Acrobacter	
• Leptospira	
• Spiroplasma (1 OTU)	0.6% (2 indiv.)
• Fusobacterium	
• Neisseria	0.3% (1 indiv.)

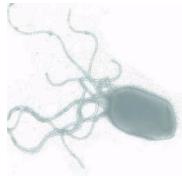




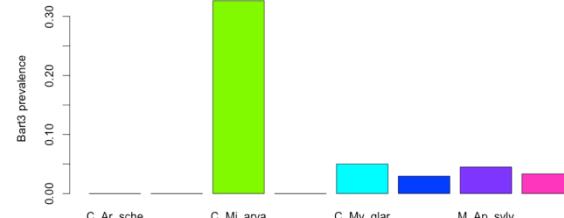
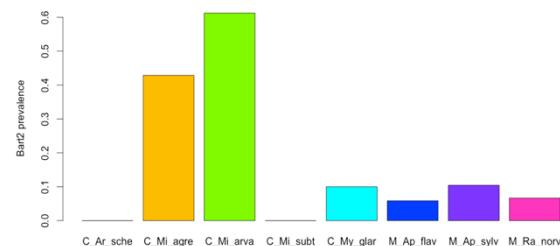
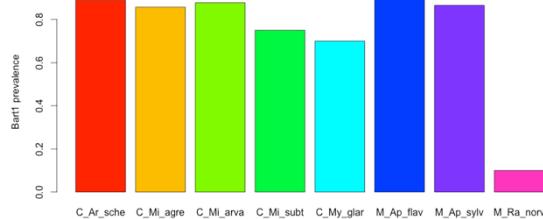
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Bartonella species : *Bartonella grahamii*, *B. doshiae*



Aryicola scherman



Miodes aarestris



M. arvalis



M. suhterraneus



Myodes glareolus



Ano. flavicollis

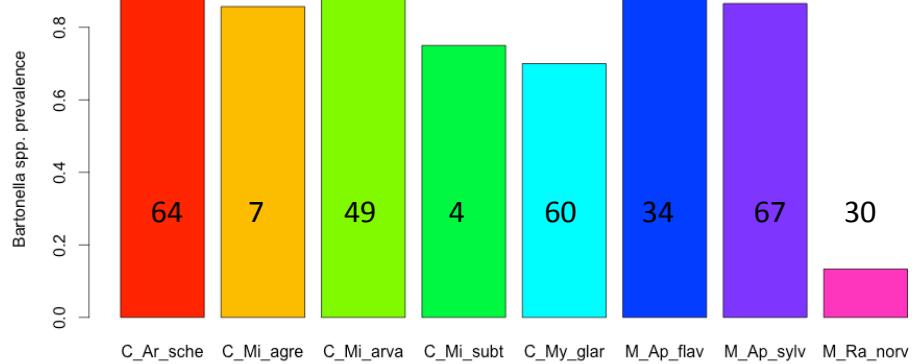


Ano. Sylvaticus

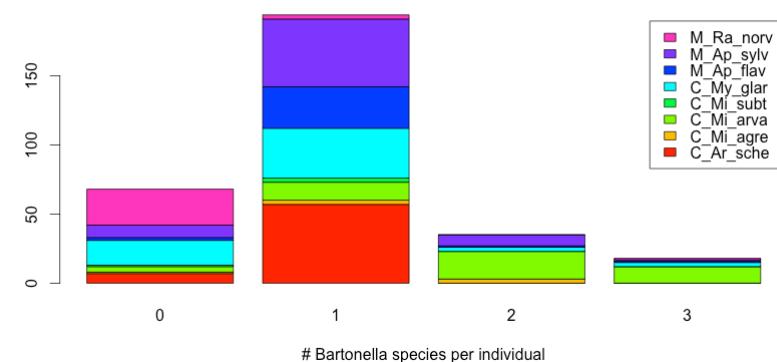


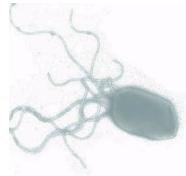
Rattus norvegicus

Overall *Bartnolla* spp. prevalence



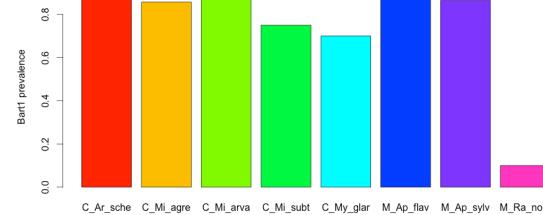
Co-infection



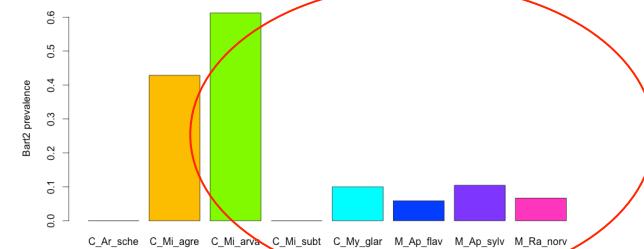


Bartonella species : *Bartonella grahamii*, *B. doshiae*

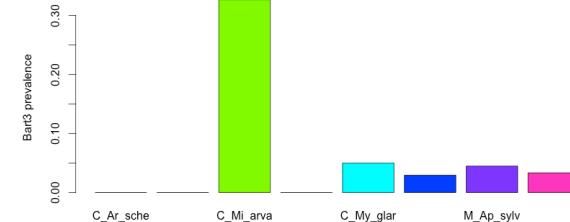
Bartonella OTU 1 (100)



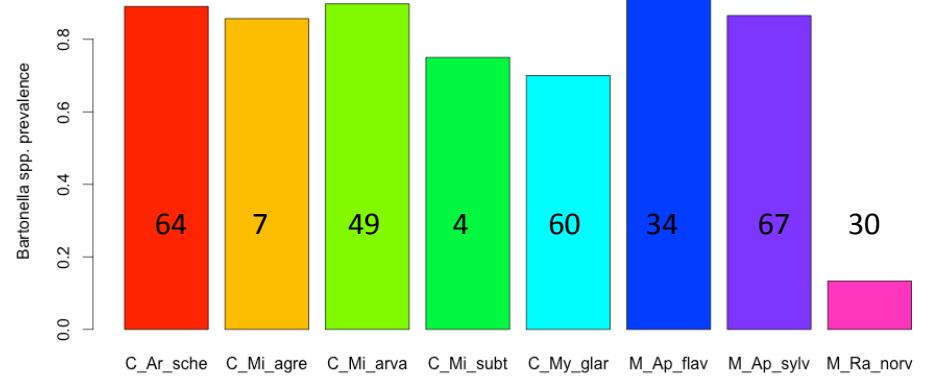
Bartonella OTU 2 (92)



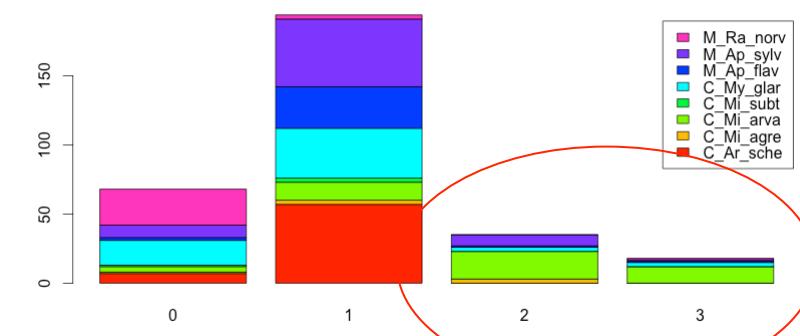
Bartonella OTU 3 (74)

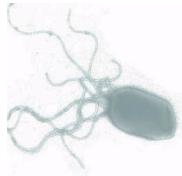


Overall *Bartnolla* spp. prevalence

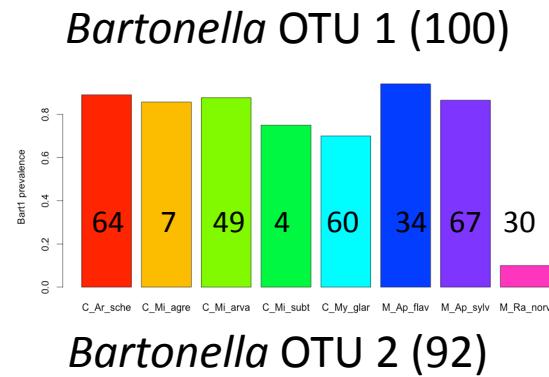


Co-infection





Bartonella species : *Bartonella grahamii*, *B. doshiae*



frontiers in
CELLULAR AND INFECTION MICROBIOLOGY

ORIGINAL RESEARCH ARTICLE
published: 15 May 2014
doi: 10.3389/fcimb.2014.00062



To be or not to be associated: power study of four statistical modeling approaches to identify parasite associations in cross-sectional studies

Elise Vaumourin^{1,2*}, Gwenaël Vourc'h¹, Sandra Telfer³, Xavier Lambin³, Diaeldin Salih⁴, Ulrike Seitzer⁵, Serge Morand^{6,7}, Nathalie Charbonnel⁸, Muriel Vayssier-Taussat² and Patrick Gasqui¹

¹ INRA, UR346 Épidémiologie Animale, Saint Genès Champanelle, France

² INRA-Anses-ENVA, USC BIPAR, Maisons-Alfort, France

³ School of Biological Sciences, University of Aberdeen, Aberdeen, UK

⁴ Department of Ticks and Tick-borne Diseases, Veterinary Research Institute, Khartoum, Sudan

⁵ Division of Veterinary-Infection Biology and Immunology, Research Center Borstel, Borstel, Germany

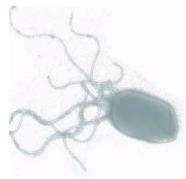
⁶ Institut des Sciences de l'Evolution (CNRS /IRD / UM2), University of Montpellier 2, Montpellier, France

⁷ Animal et Gestion Intégrée des Risques, CIRAD, Montpellier, France

⁸ INRA, UMR CBGP (INRA / IRD / CIRAD / Montpellier SupAgro), Montpellier, France

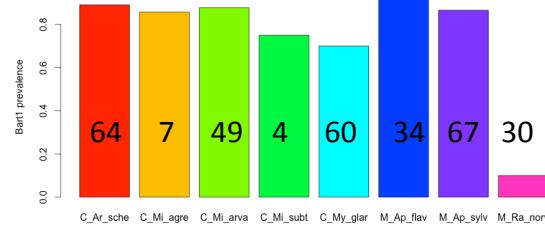
Vaumourin *et al.* 2014
Association Screening Index



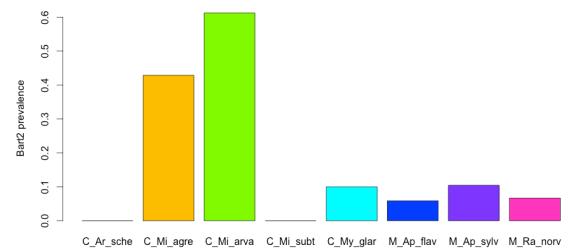


Bartonella species : *Bartonella grahamii*, *B. doshiae*

Bartonella OTU 1 (100)

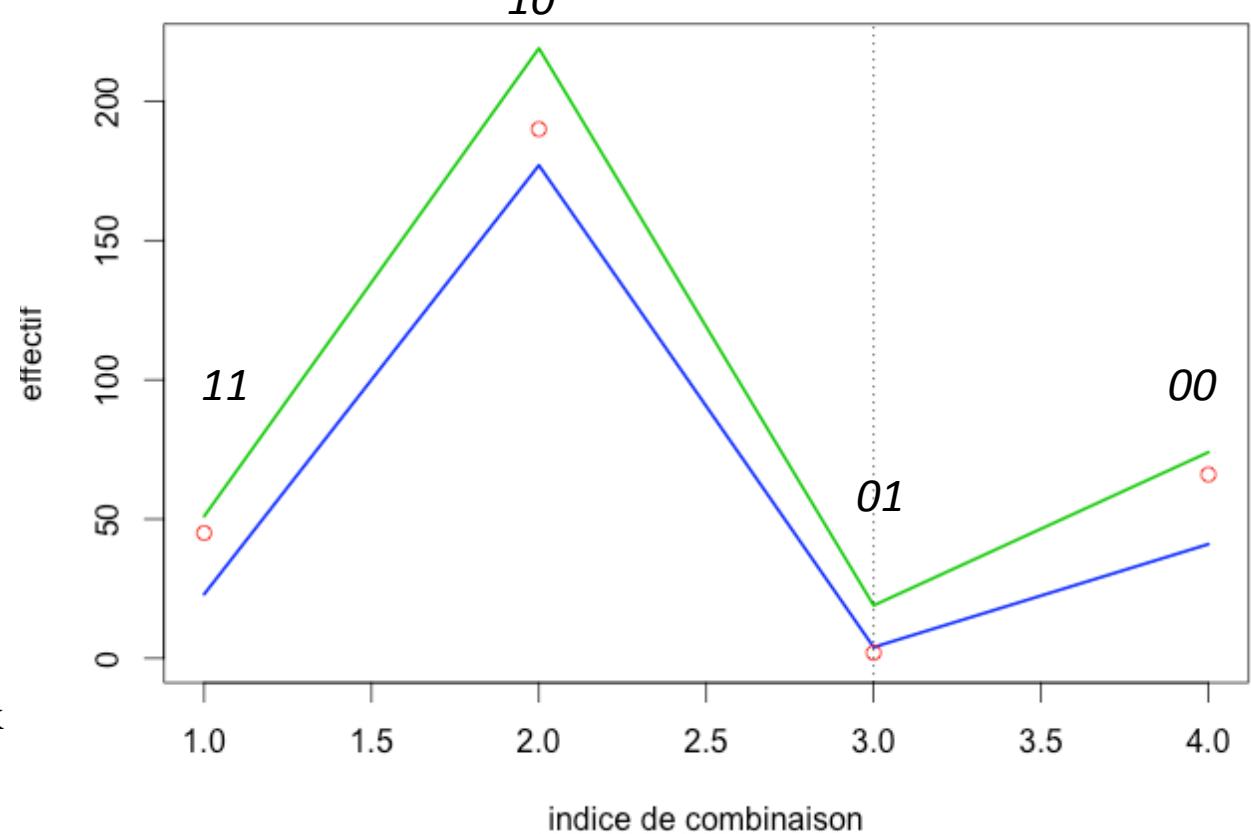


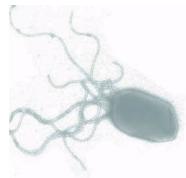
Bartonella OTU 2 (92)



Vaumourin et al. 2014
Association Screening Index

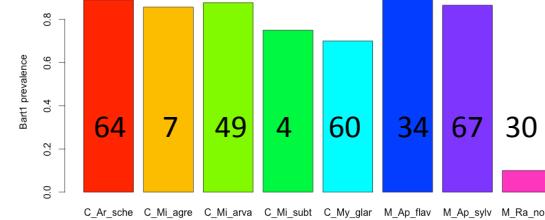
Association Obs - +
01 2 4 19 p = 1 0.0020





Bartonella species : *Bartonella grahamii*, *B. doshiae*

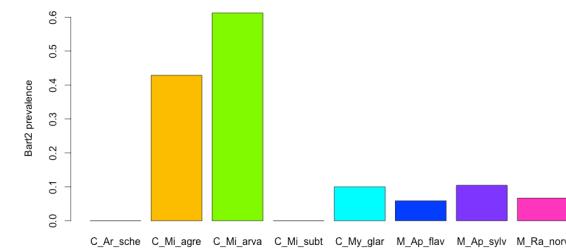
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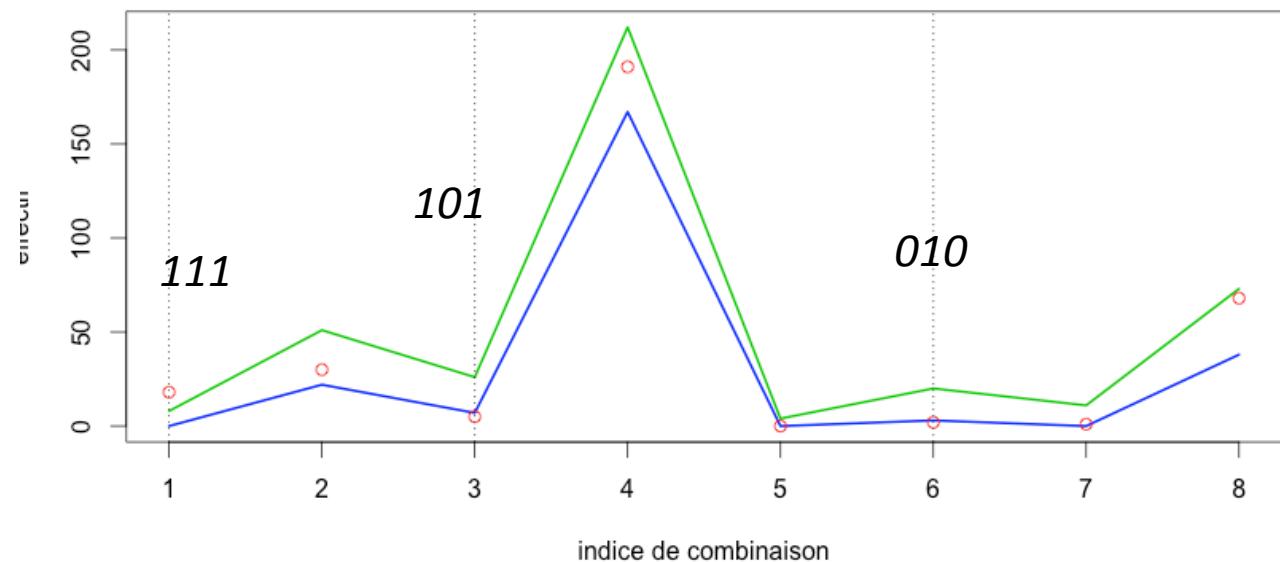
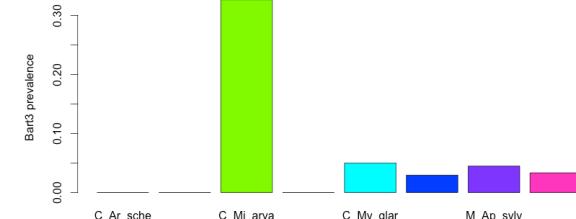
Association Obs - +

111	18	0	8	p = 0.0000
101	5	7	26	p = 0.0020
010	2	3	20	p = 0.0036
001	1	1	0	p = 0.2152

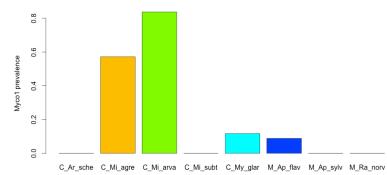
Bartonella OTU 2 (92)



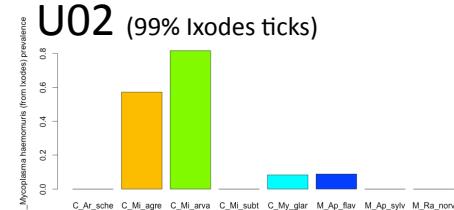
Bartonella OTU 3 (74)



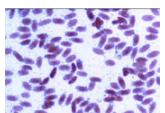
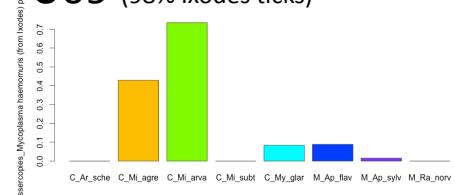
1 (99% Ixodes ticks)



U02 (99% Ixodes ticks)



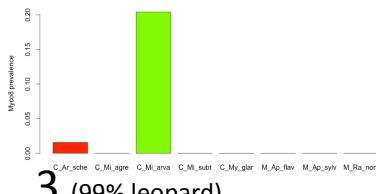
U09 (98% Ixodes ticks)



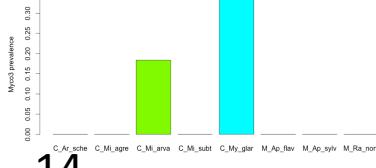
**19+ independent
Mycoplasma OTUs**

- M_Ra_nov
- M_Ap_sylv
- M_Ap_flav
- C_My_glar
- C_Mi_subt
- C_Mi_arva
- C_Mi_agre
- C_Ar_sche

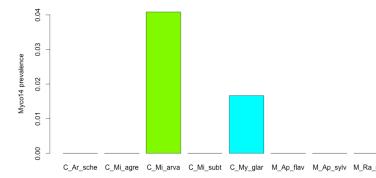
8 (95% bat)



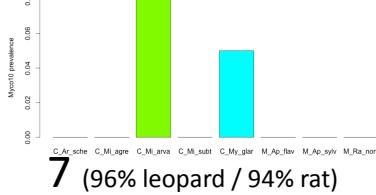
3 (99% leopard)



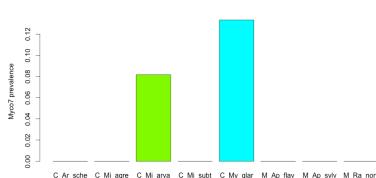
14



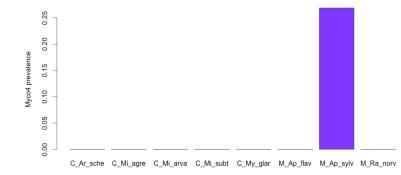
10 (96% leopard / 94% bat)



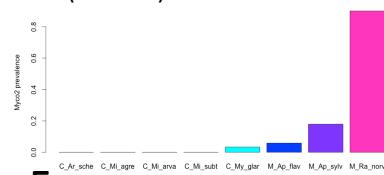
7 (96% leopard / 94% rat)



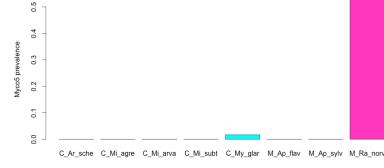
4 (99% mouse/ M.haemofelis)



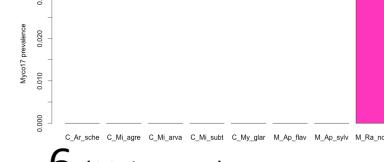
2 (99% rat)



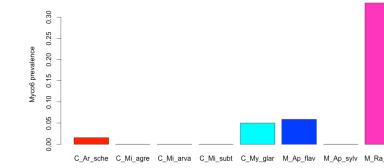
5 (100% rat)



17 (99% rat)



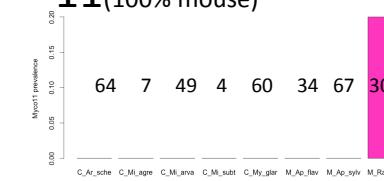
6 (99% mouse)



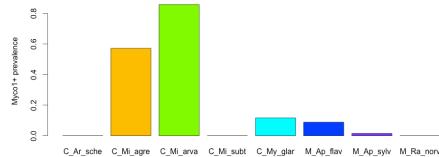
15 (100% murine)



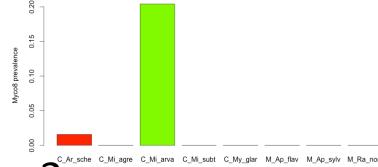
11(100% mouse)



1+ (99% Ixodes ticks)



8 (95% bat)



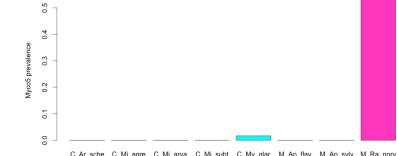
4+ (99% mouse/ M.haemofelis)

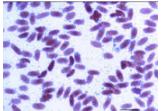


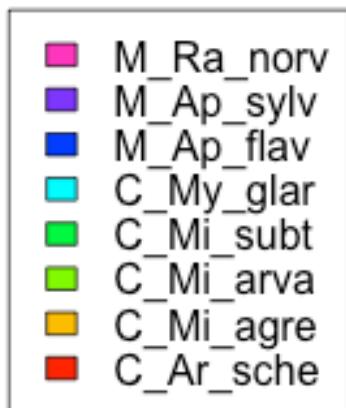
2 (99% rat)



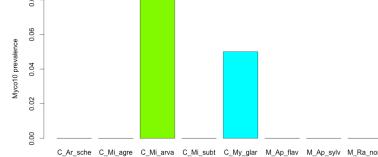
5 (100% rat)



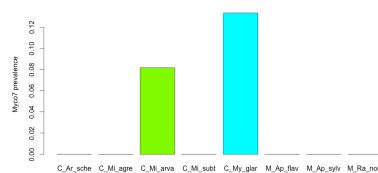
 **Most likely ~12 Mycoplasma spp.**



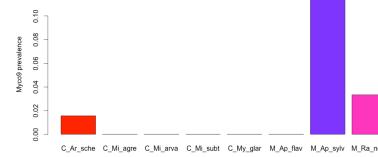
10 (96% leopard / 94% bat)



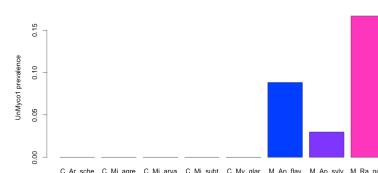
7 (96% leopard / 94% rat)



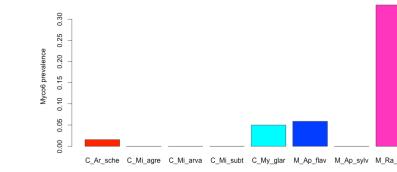
9



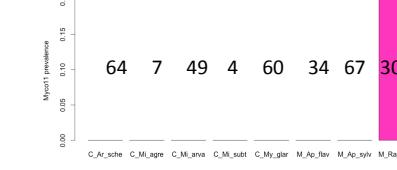
U12 (93% leopard and murine)



6 (99% mouse)



11 (100% mouse)



Arvicola scherman



Miodes agrestris



M. arvalis



M. subterraneus



Myodes glareolus



Apo. flavicollis



Apo. Sylvaticus

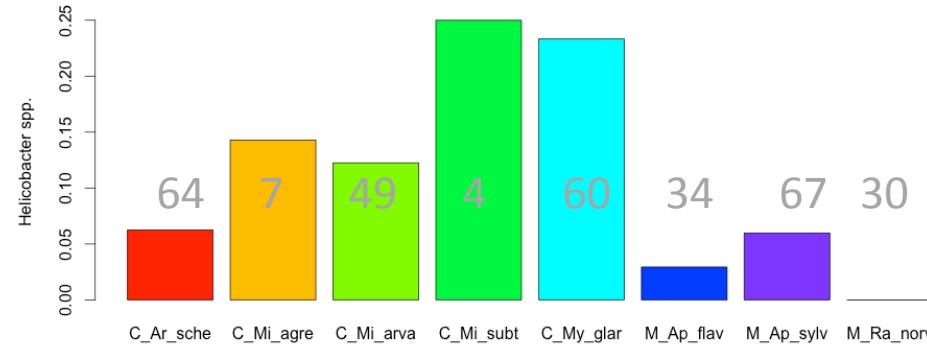


Rattus norvegicus

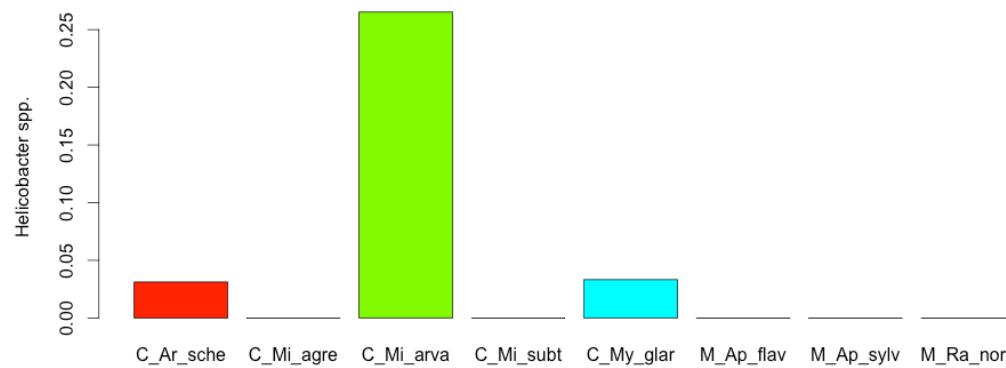


Helicobacter species : *H.suncus* + *H. trogontum* isolated from shrews and other mammals with chronic gastritis

Helicobacter OTU 1(100)



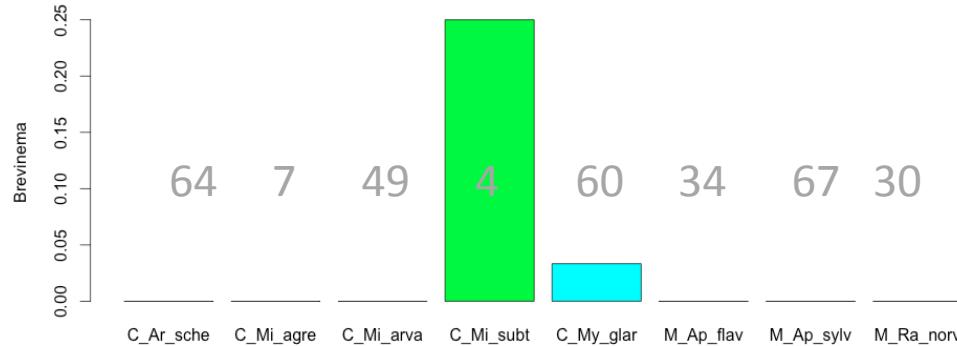
Helicobacter OTU 2 (100)





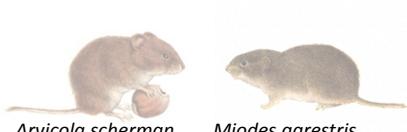
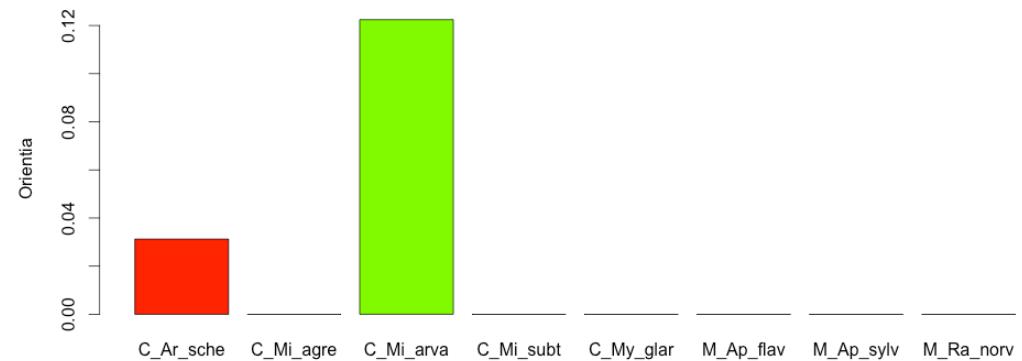
Brevinema (100)

97% homology to *B. andersonii* spirochaete of short-tailed shrew (*Blarina brevicauda*) & white-footed mouse (*P. leucopus*) in N. America



Orientia (100)

100% homology to rickettsial *O. tsutsugamushi* causing zoonotic scrub typhus; here, found only among meadow voles



Arvicola scherman



Miodes agrestis



M. arvalis



M. subterraneus



Myodes glareolus



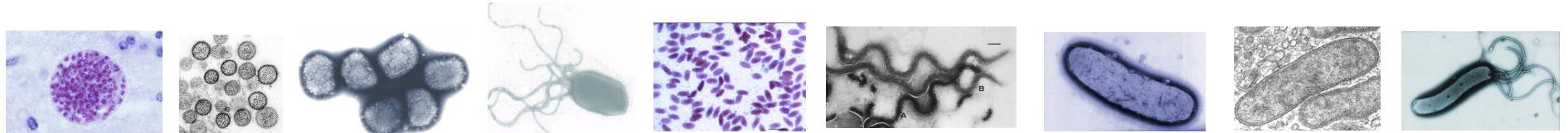
Apo. flaviculus



Apo. Sylvaticus



Rattus norvegicus



3 viruses (historical)

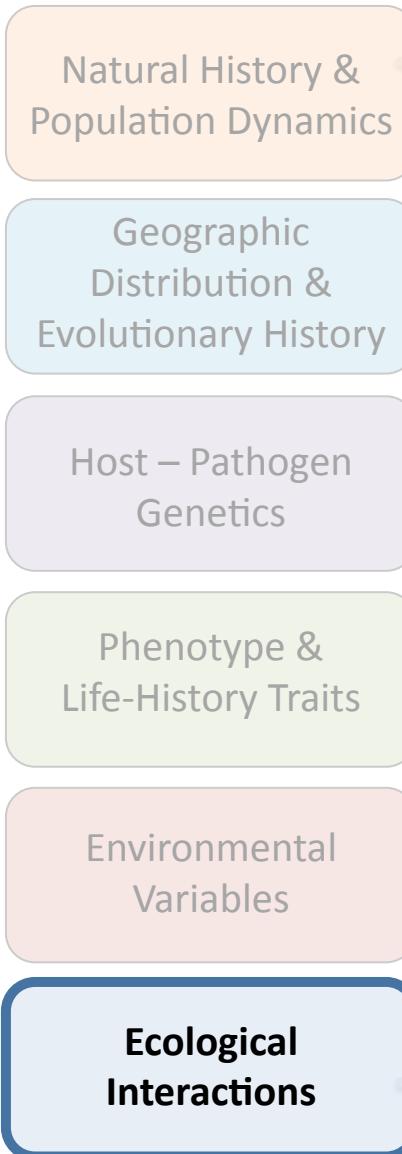
2? protazoa

15-31 bacteria species

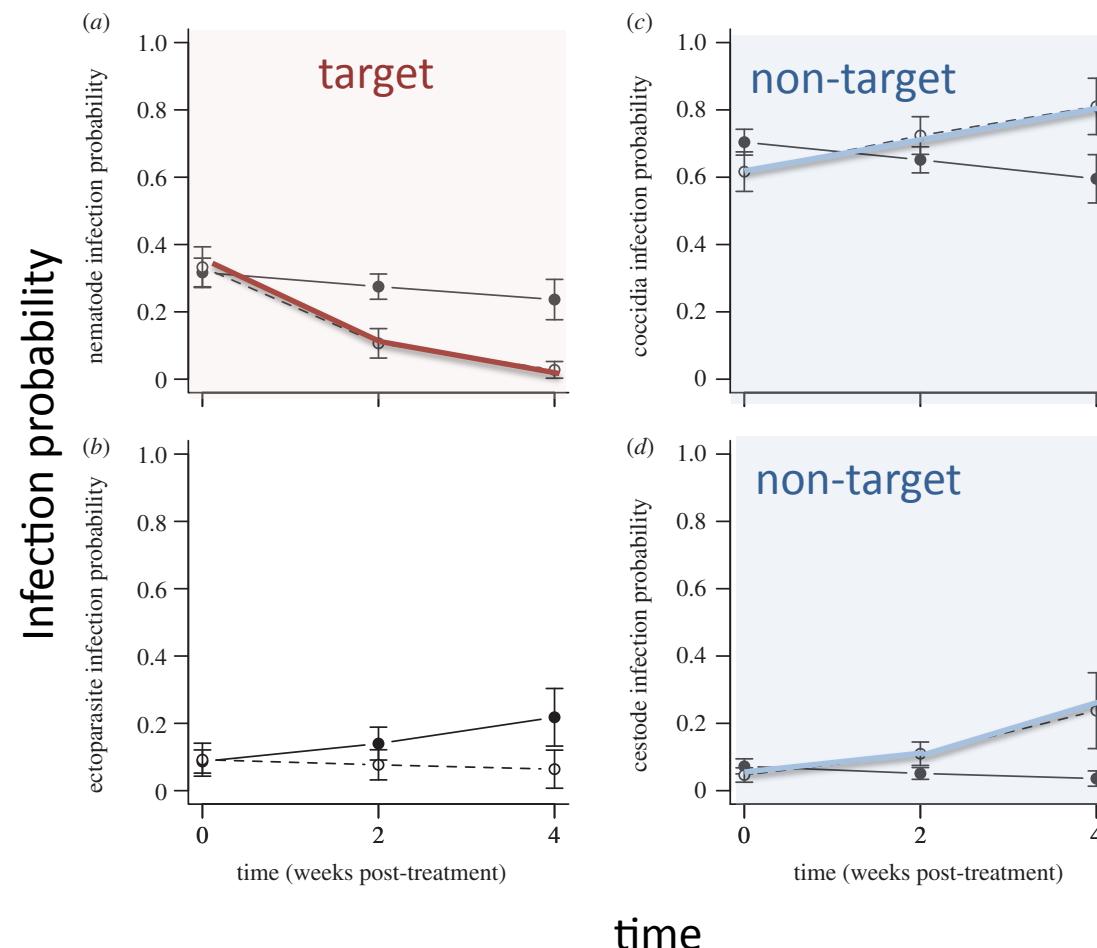
✓ Host species is the main determinant of among - individual presence for any one parasite.



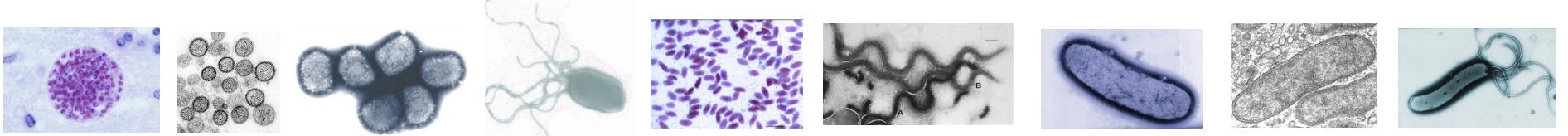
Co-infection Patterns



Parasite removal experiment demonstrates competitive exclusion between gut parasites of *Peromyscus* spp. in the United States



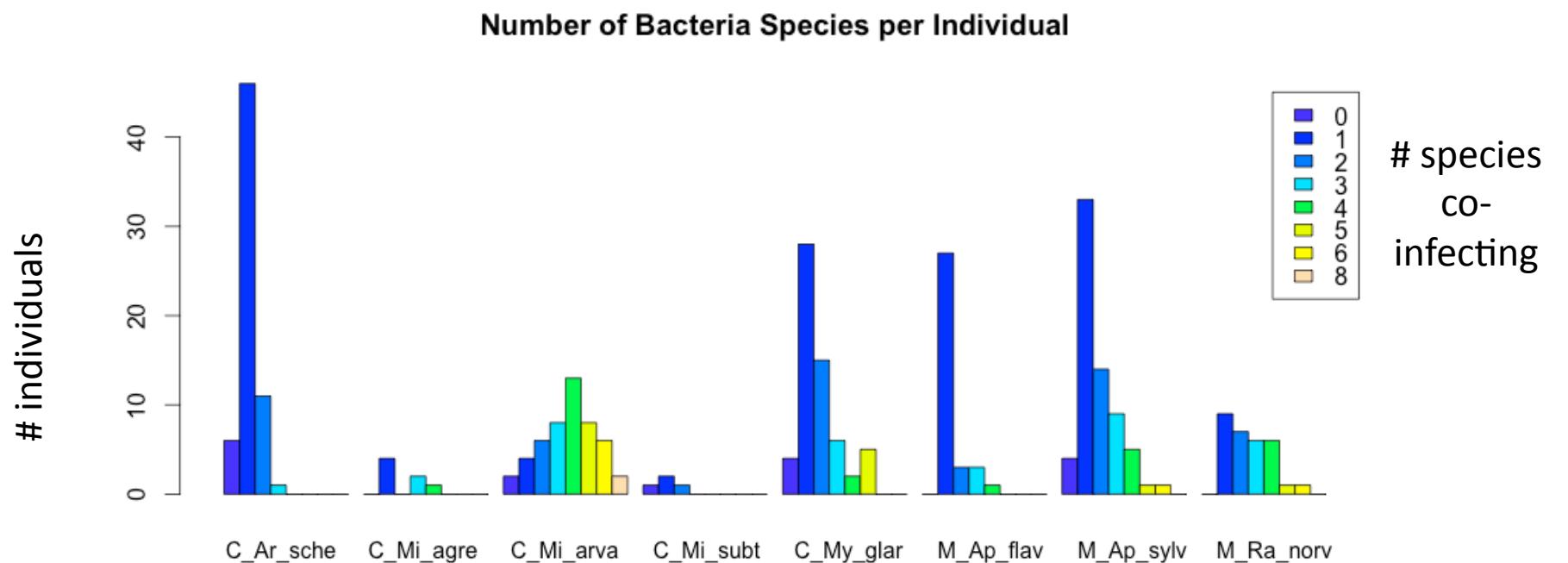
Pedersen & Antonovics 2013 *Biol Letters*



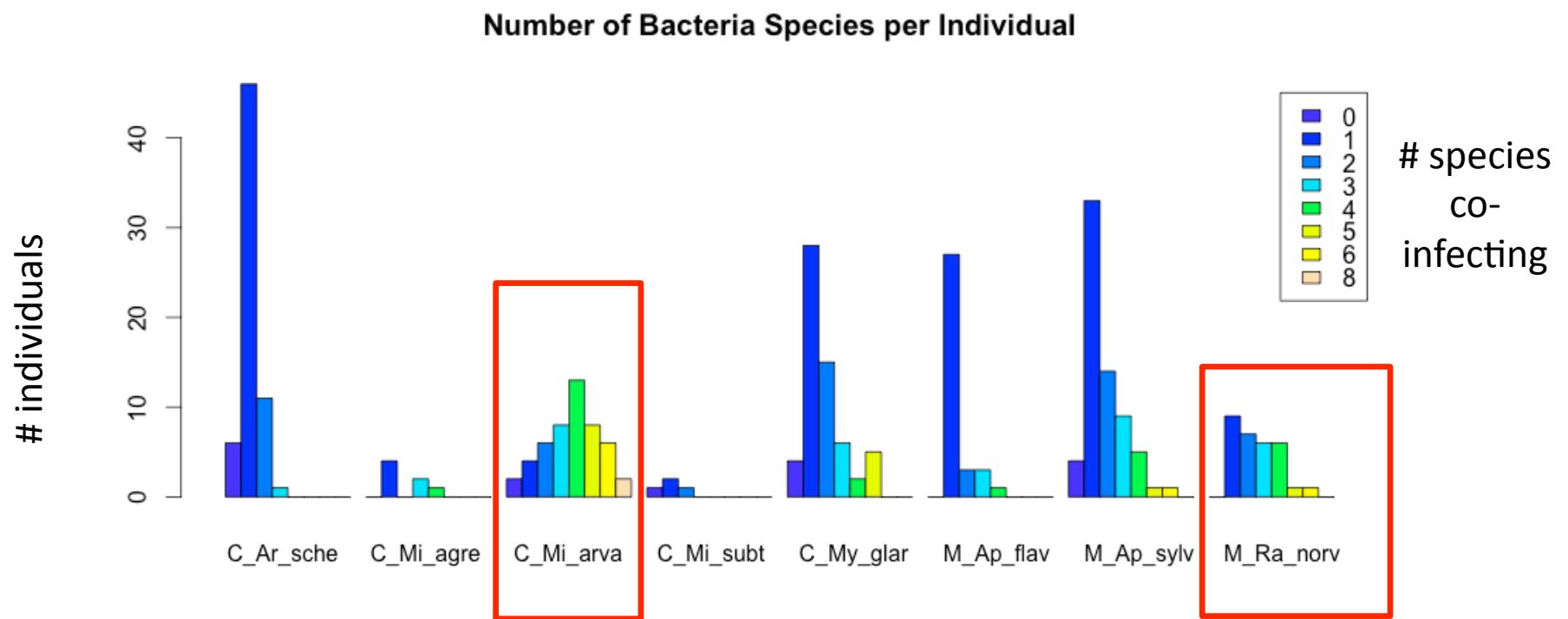
Co-infection Patterns

Do co-infections occur?
What determines co-infection rates?
Are there associations (+ & -) between
parasites (or a history thereof)?

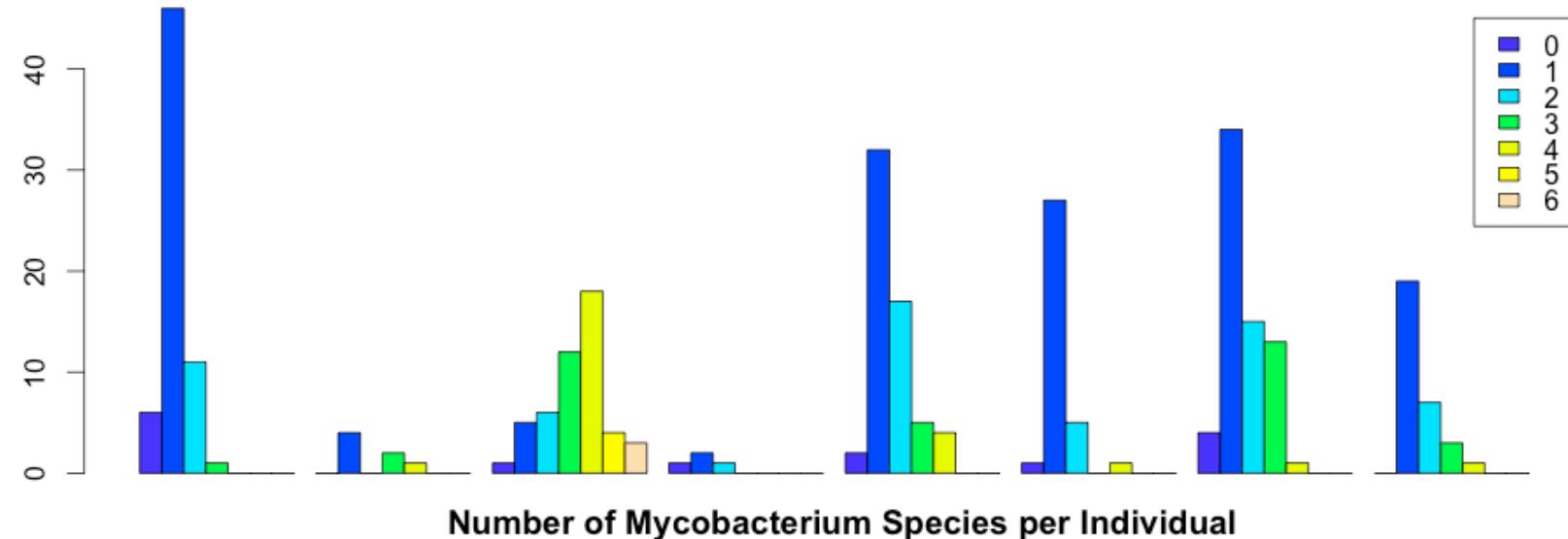




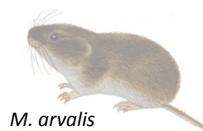
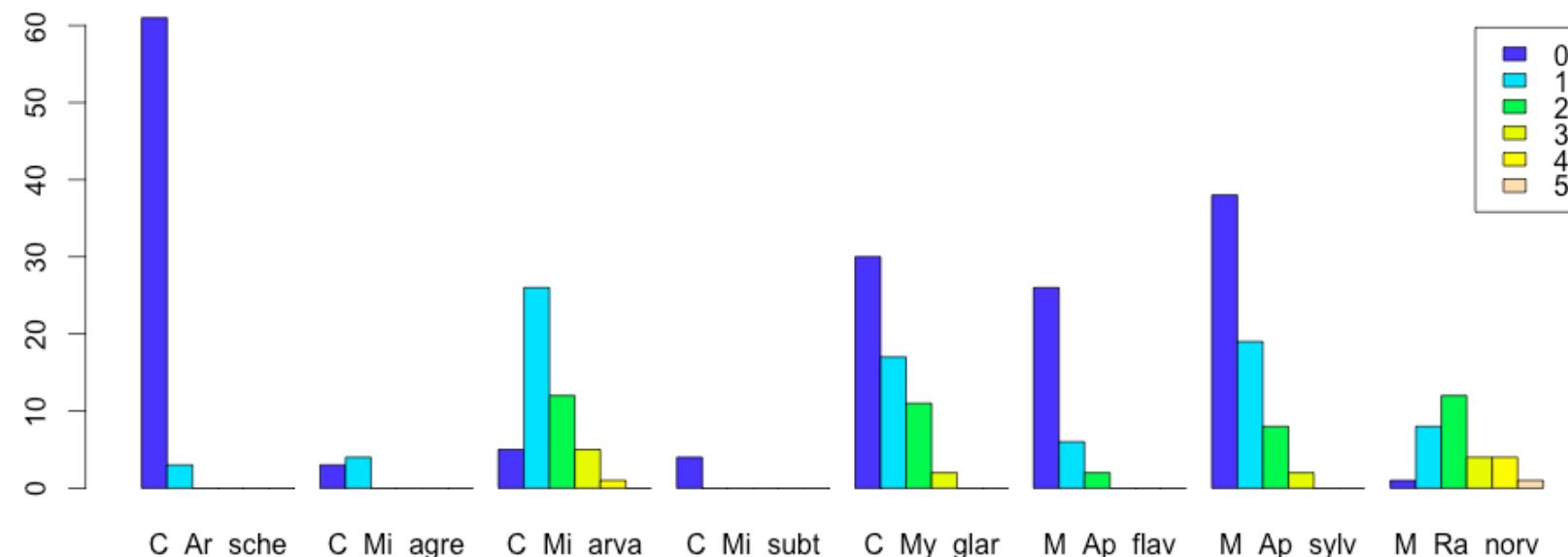
species
co-
infecting



Number of Bacteria Species (indep. of Mycobacteria) per Individual



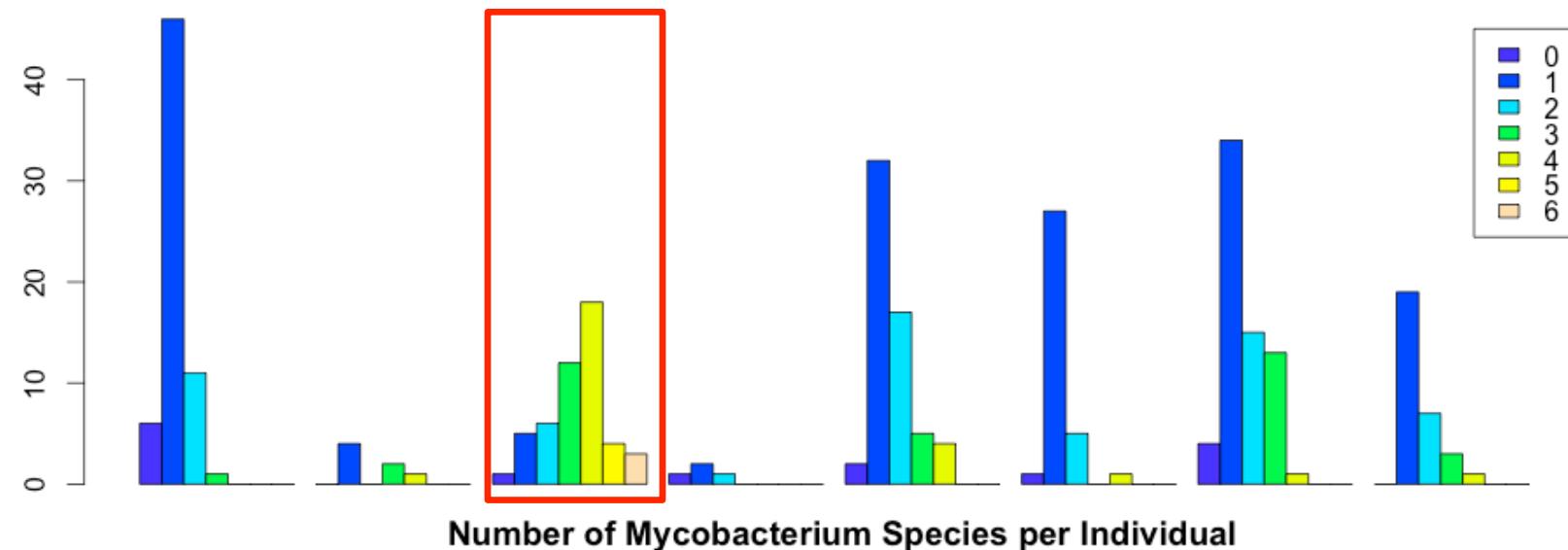
Number of Mycobacterium Species per Individual



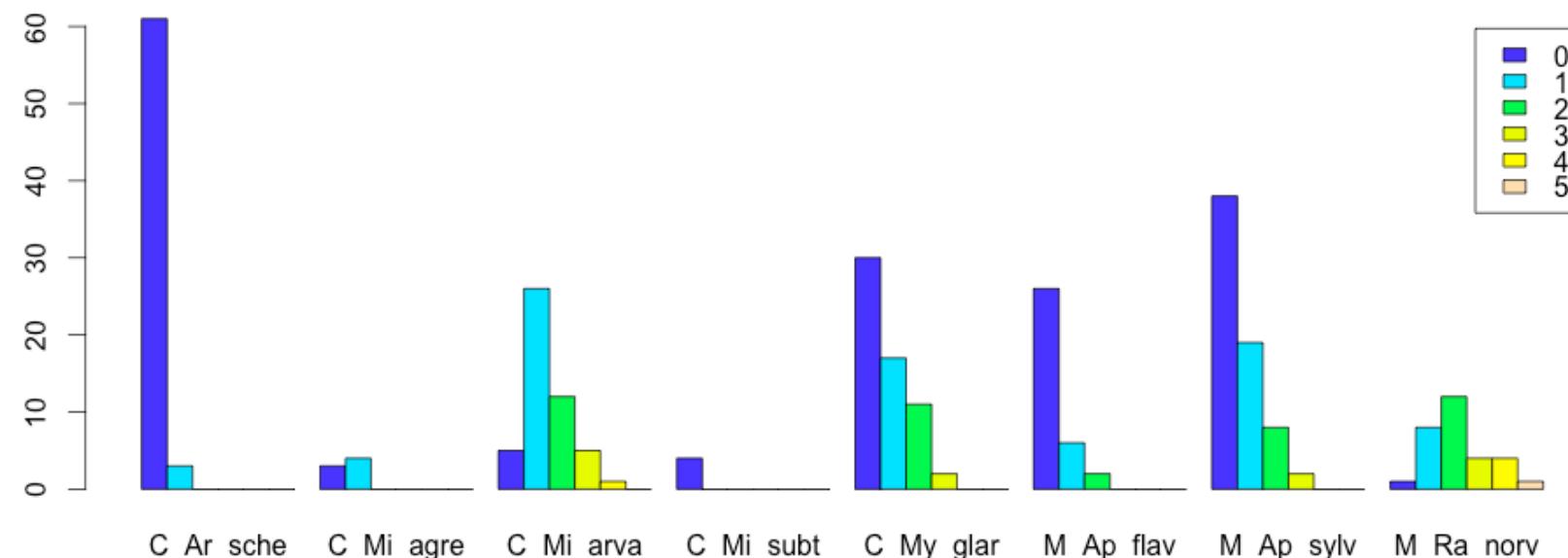
M. arvalis



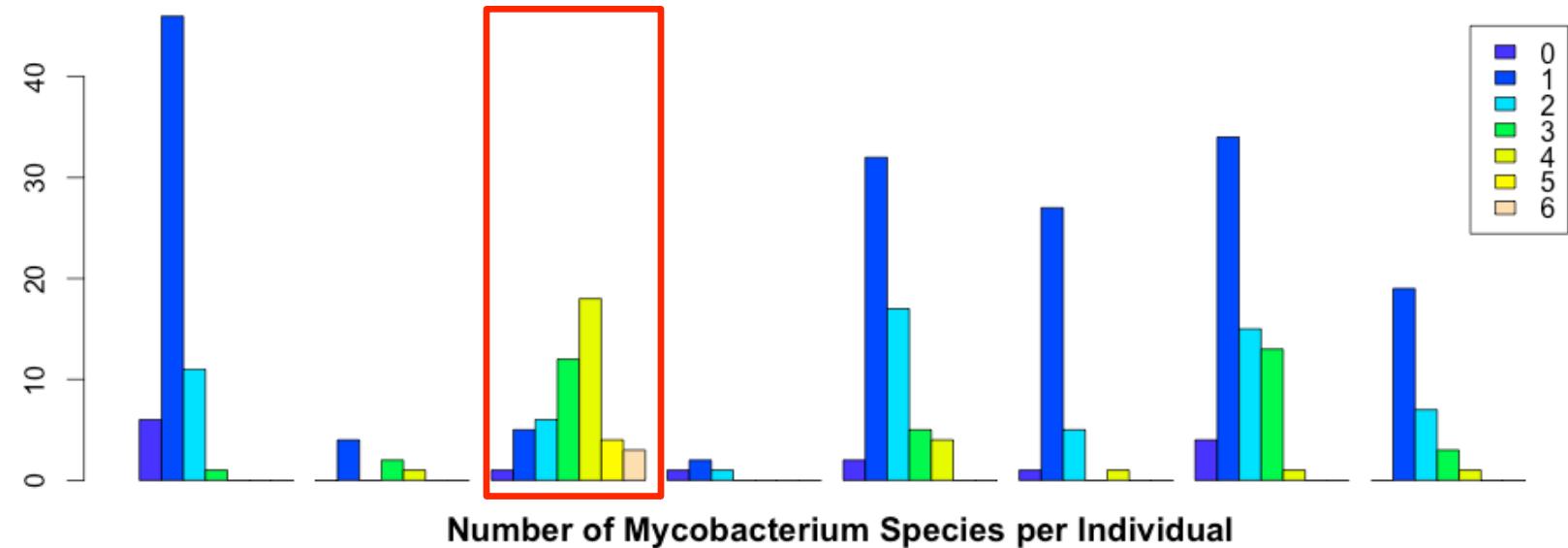
Number of Bacteria Species (indep. of Mycobacteria) per Individual



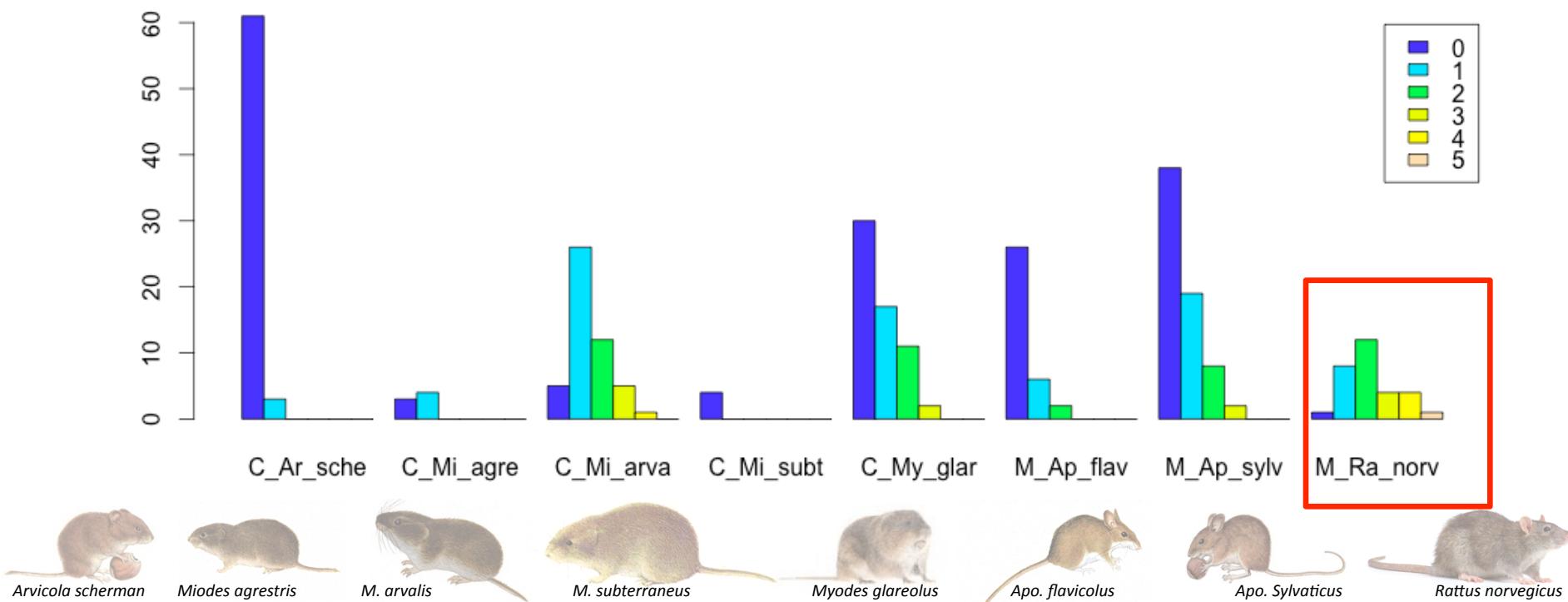
Number of Mycobacterium Species per Individual



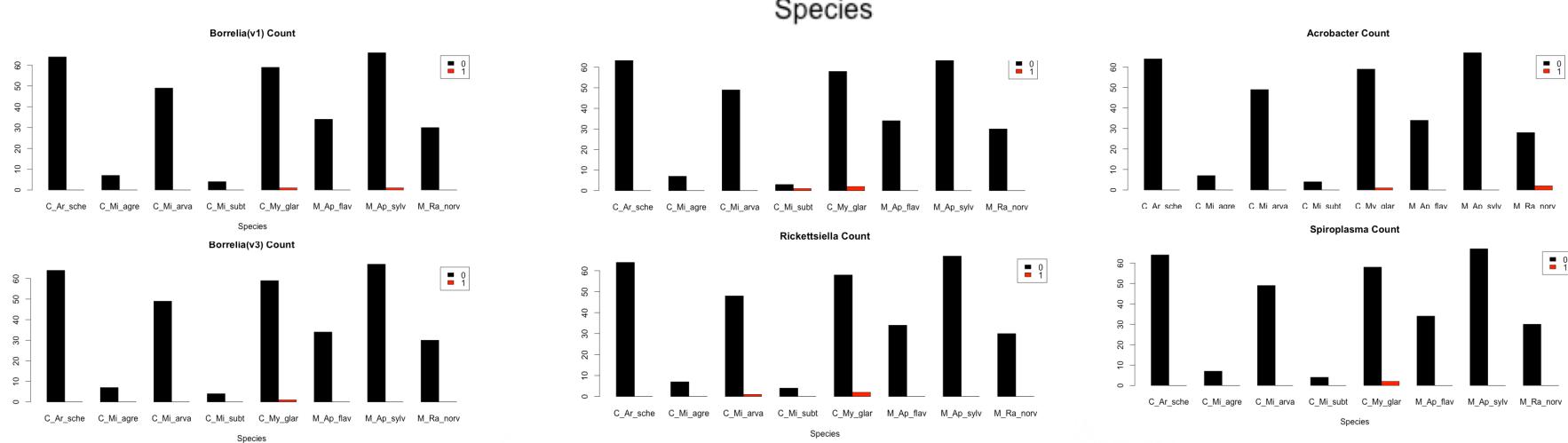
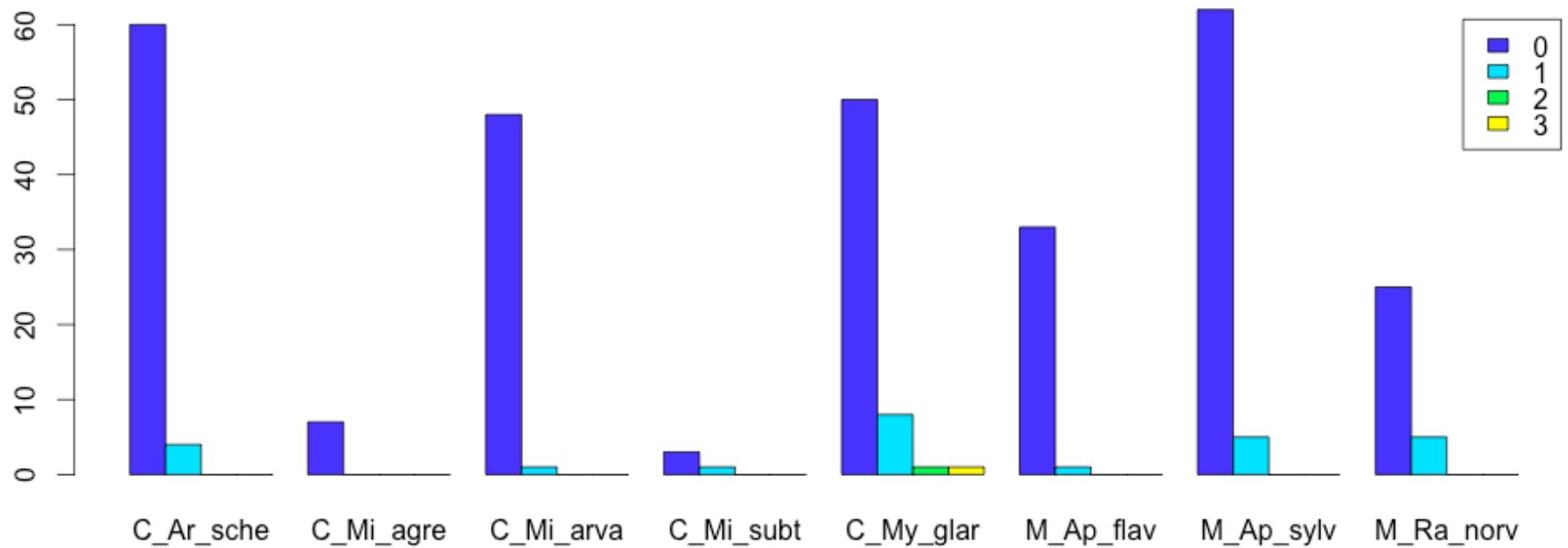
Number of Bacteria Species (indep. of Mycobacteria) per Individual



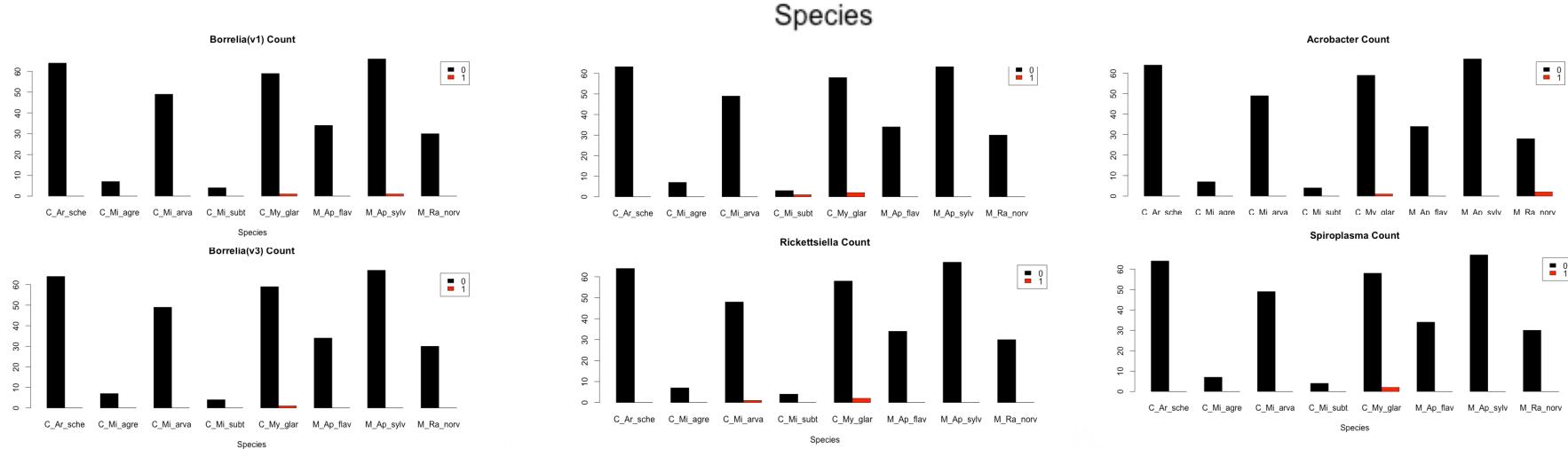
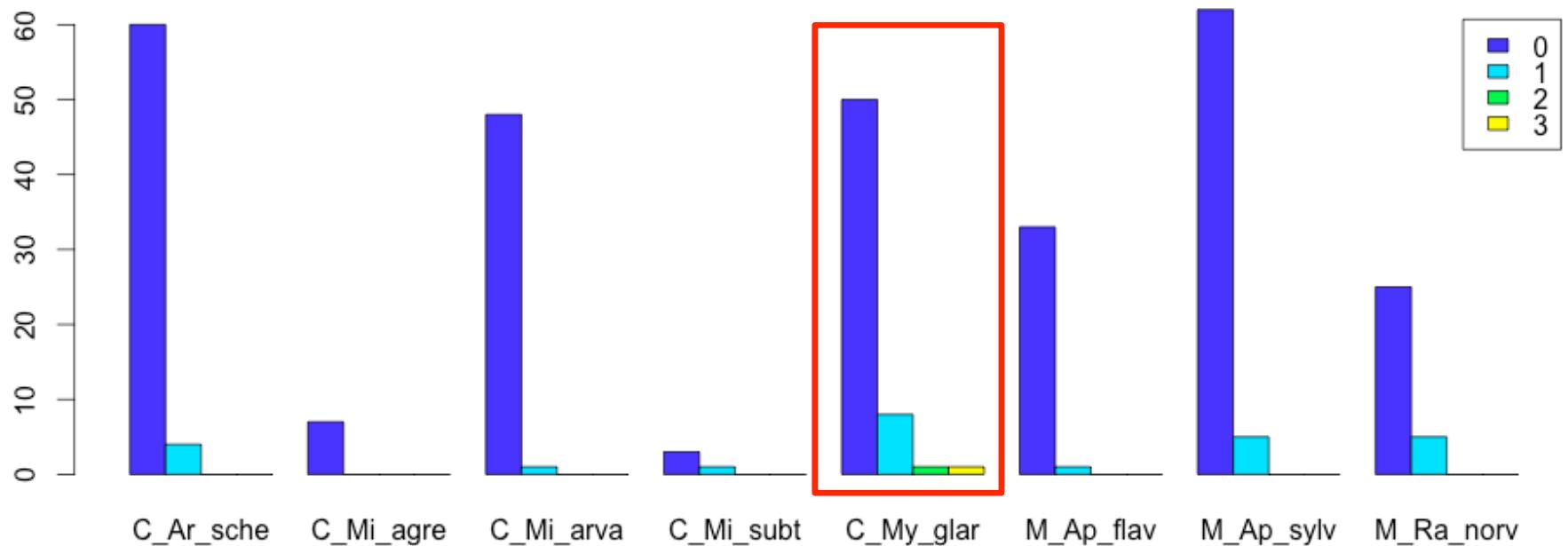
Number of Mycobacterium Species per Individual



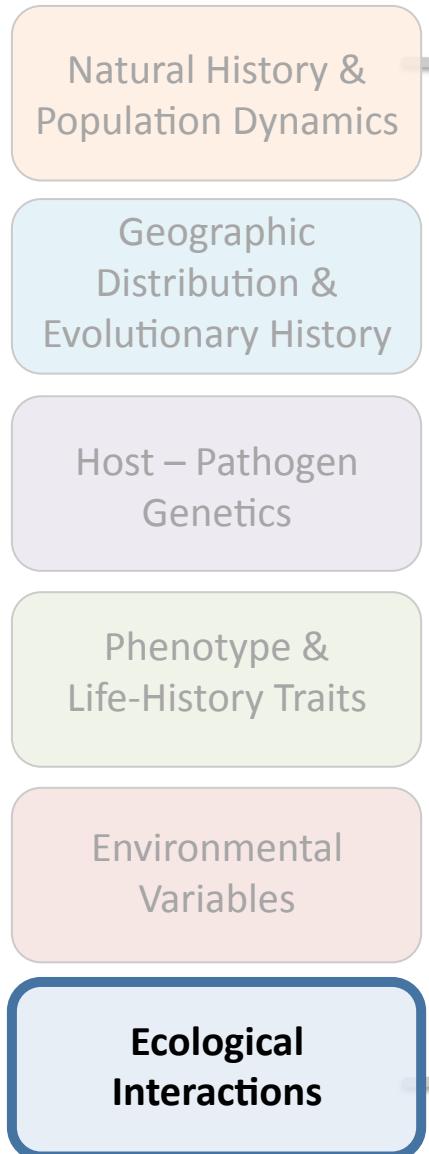
Number of Rare Bacteria Species (indep. of Mycobacteria) per Individual



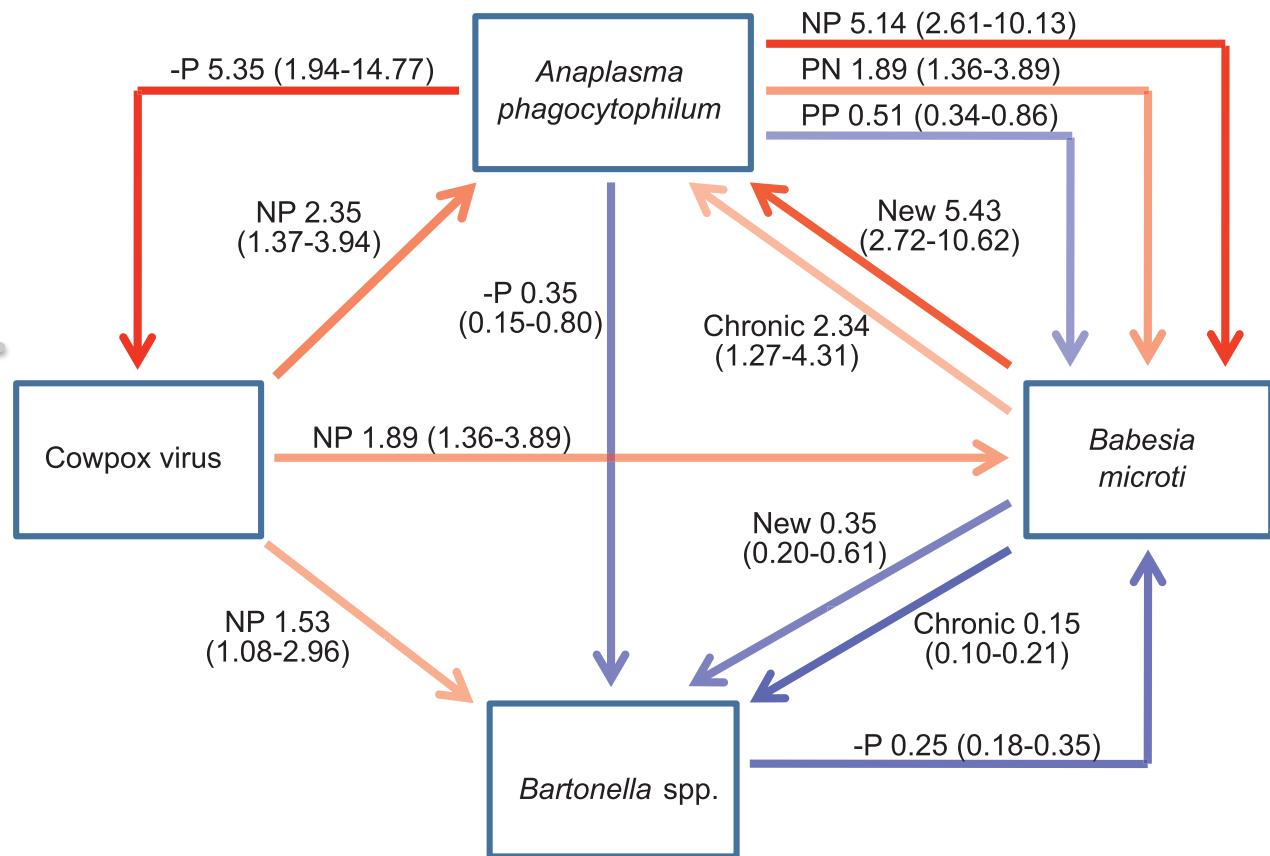
Number of Rare Bacteria Species (indep. of Mycobacteria) per Individual



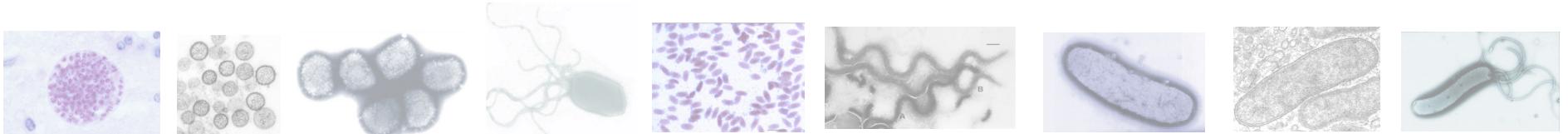
Co-infection Patterns



Cowpox (OPXV) weakly facilitates bacterial infections in 5981 *Microtus agrestis* of a UK forest



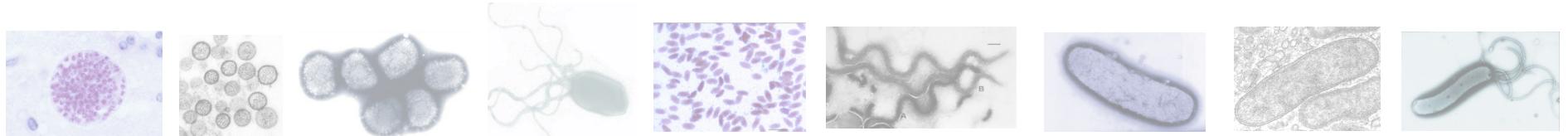
Telfer et al. 2010 *Science*



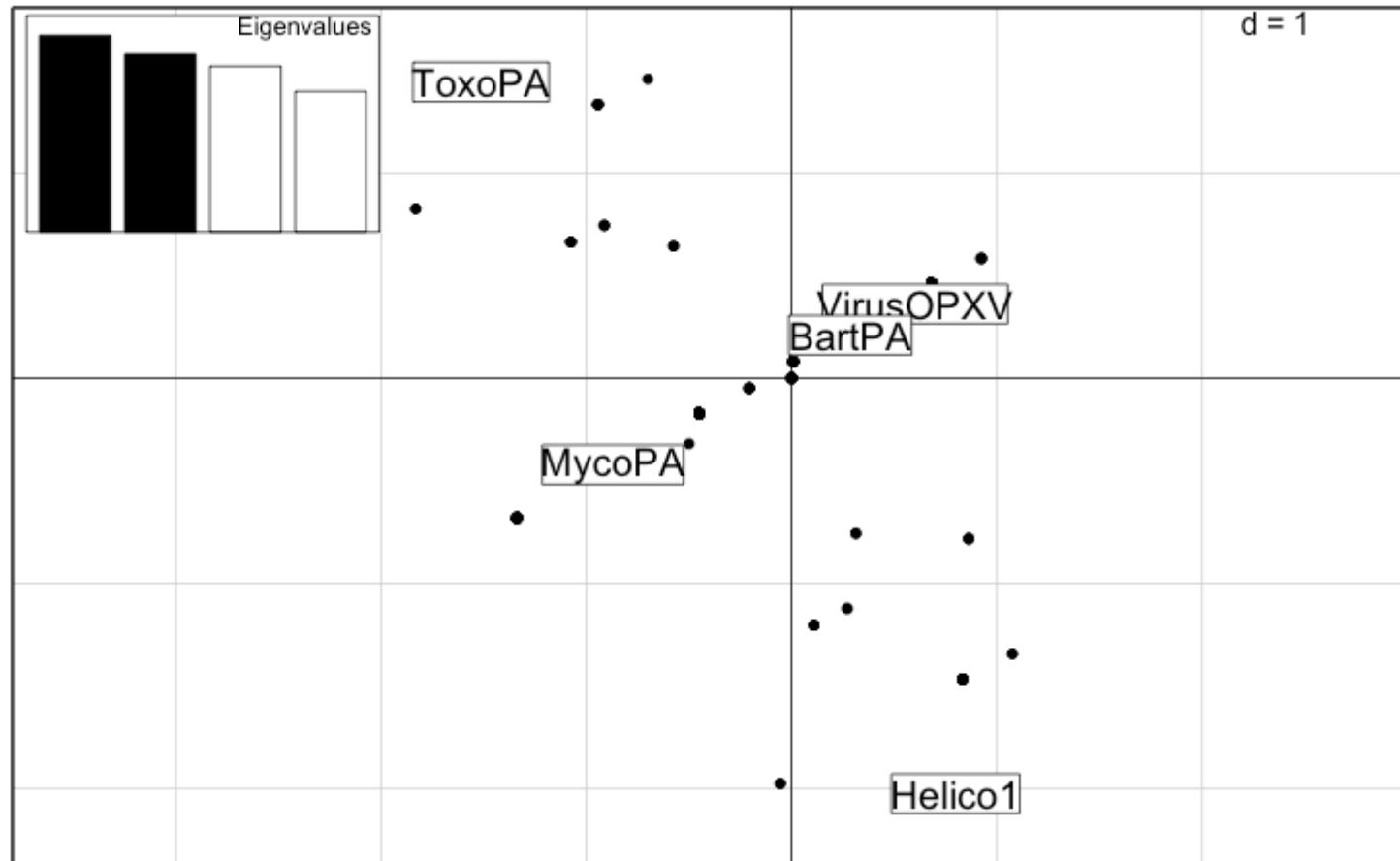
An example from our data:

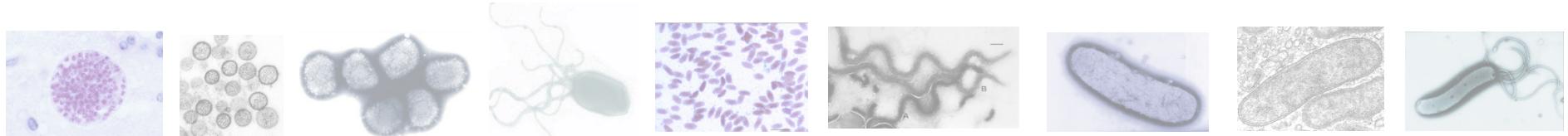
Cowpox Virus (OPXV)	33%
Bartonella (any)	78%
Mycoplasma (any)	46%
Helicobacter (1)	10%
Toxo History (Abs)	7%



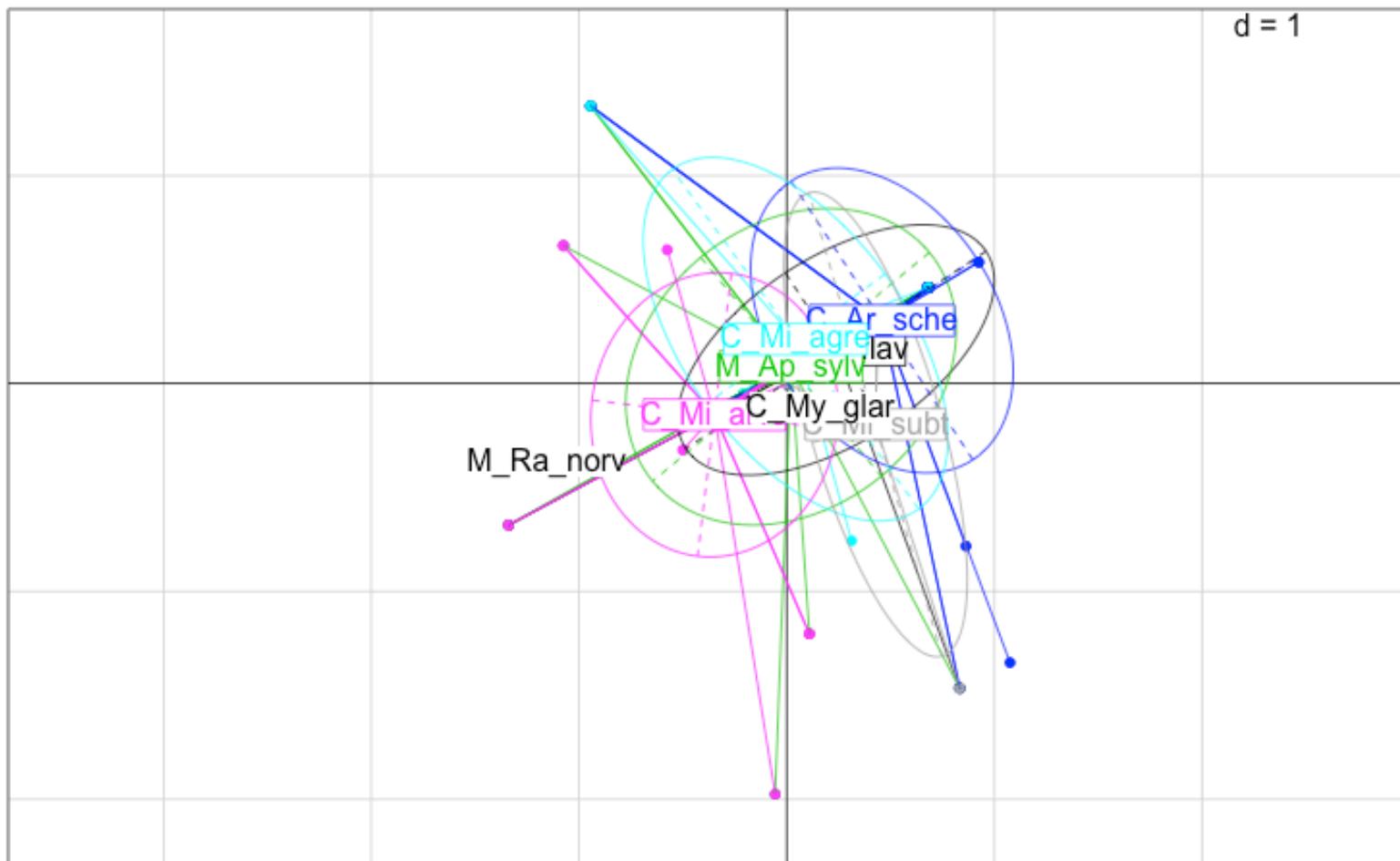


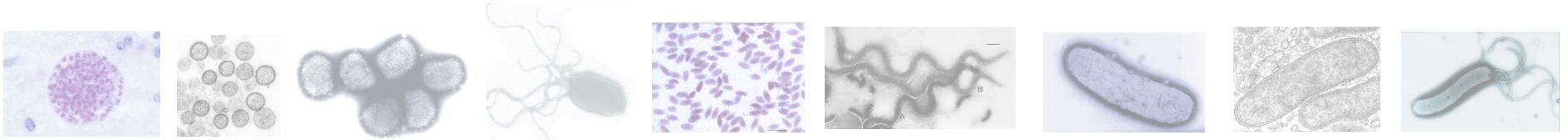
Factor Correspondence Analysis (AFC)



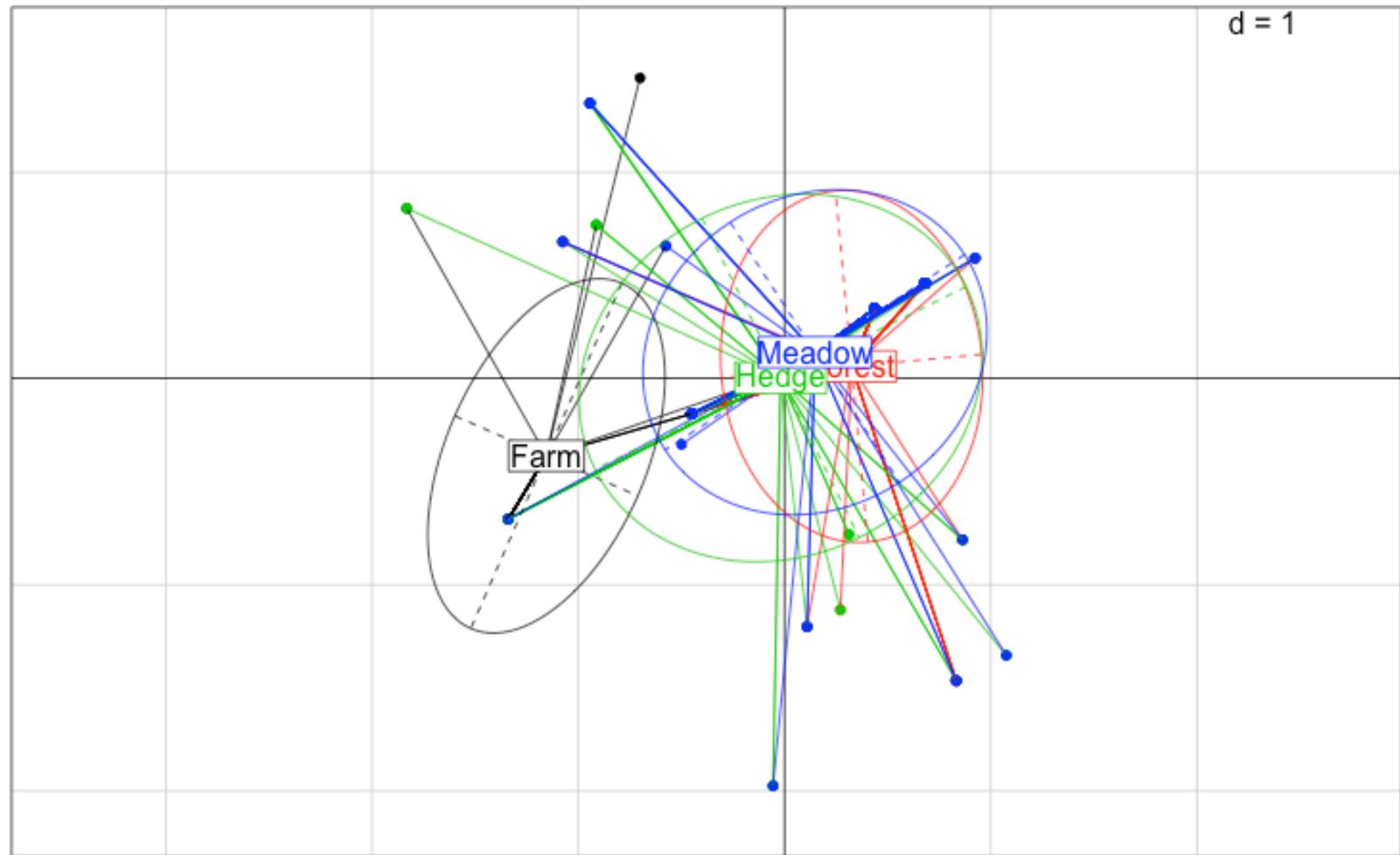


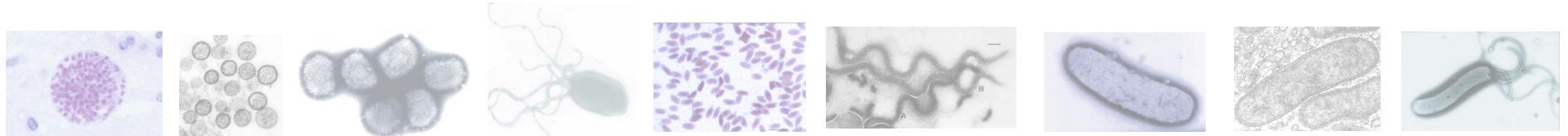
Multiple Correspondence Analysis (MCA)



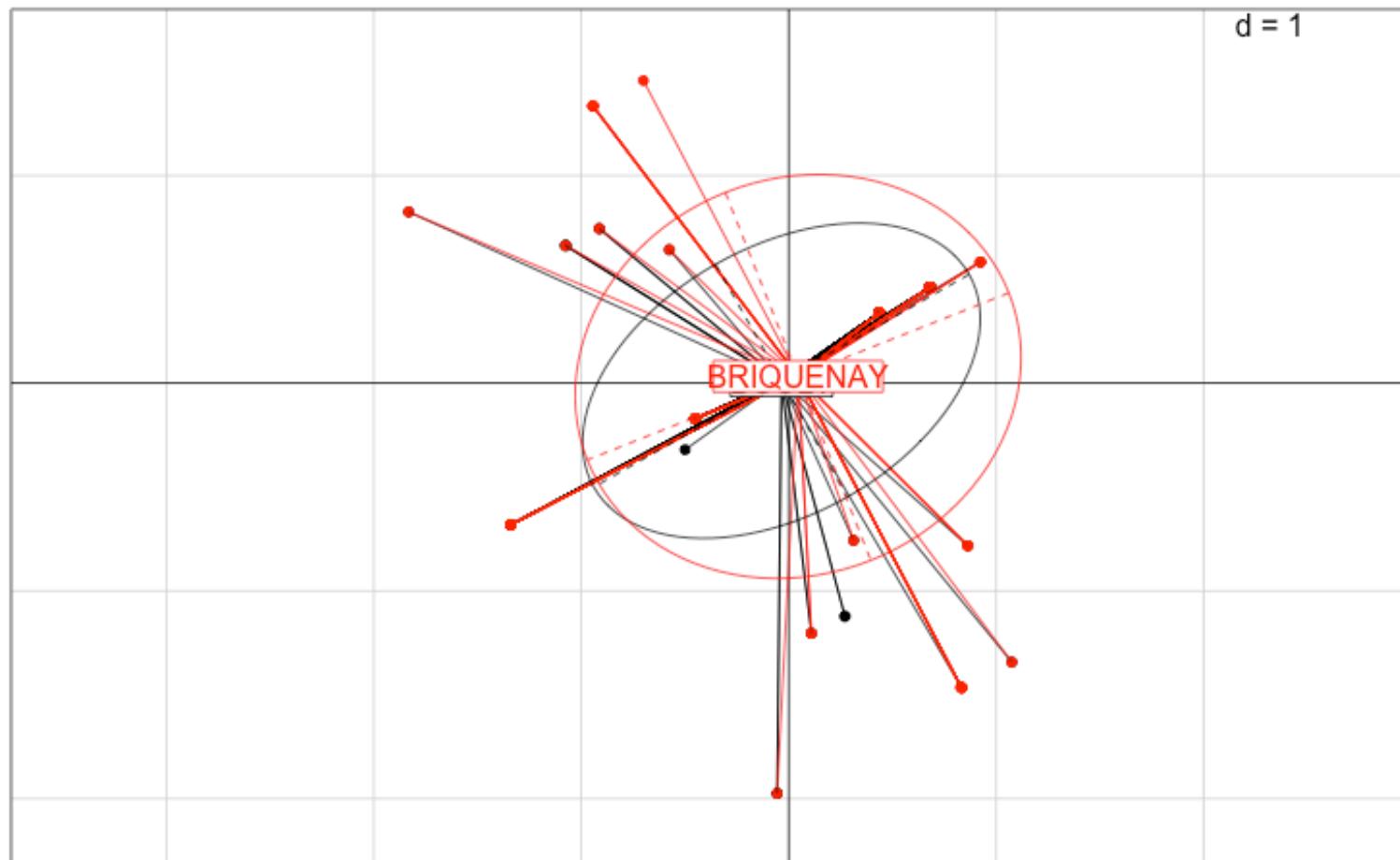


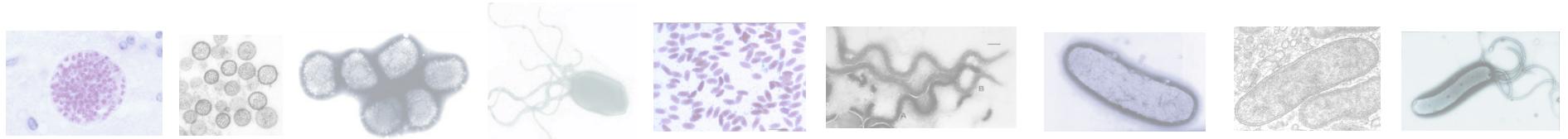
Multiple Correspondence Analysis (MCA)



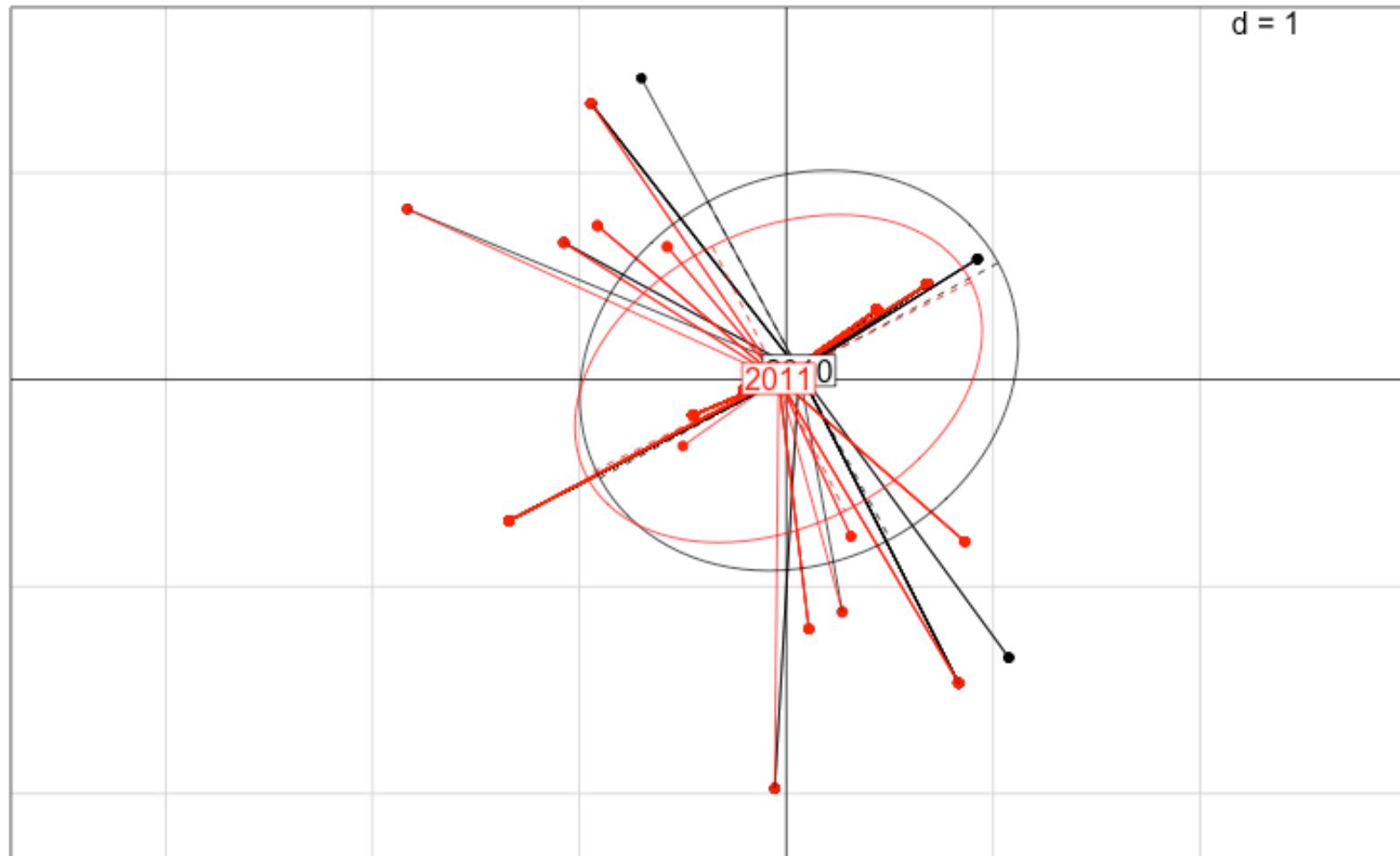


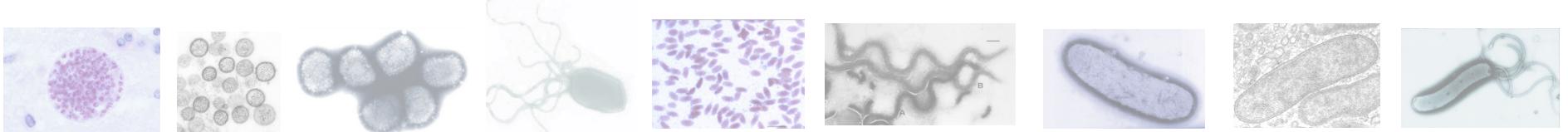
Multiple Correspondence Analysis (MCA)



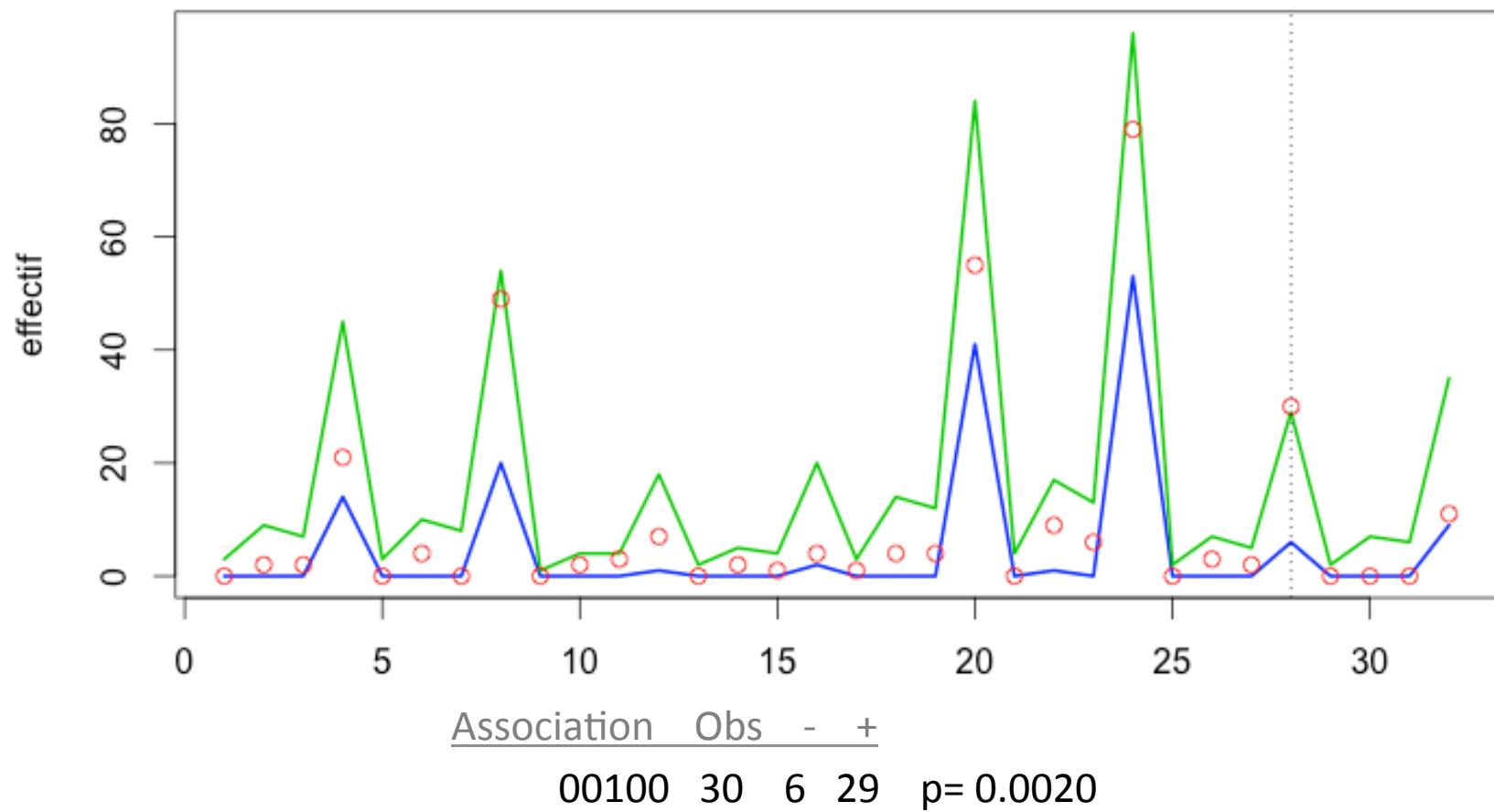


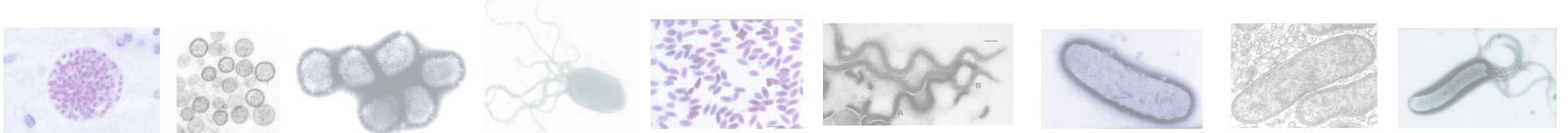
Multiple Correspondence Analysis (MCA)



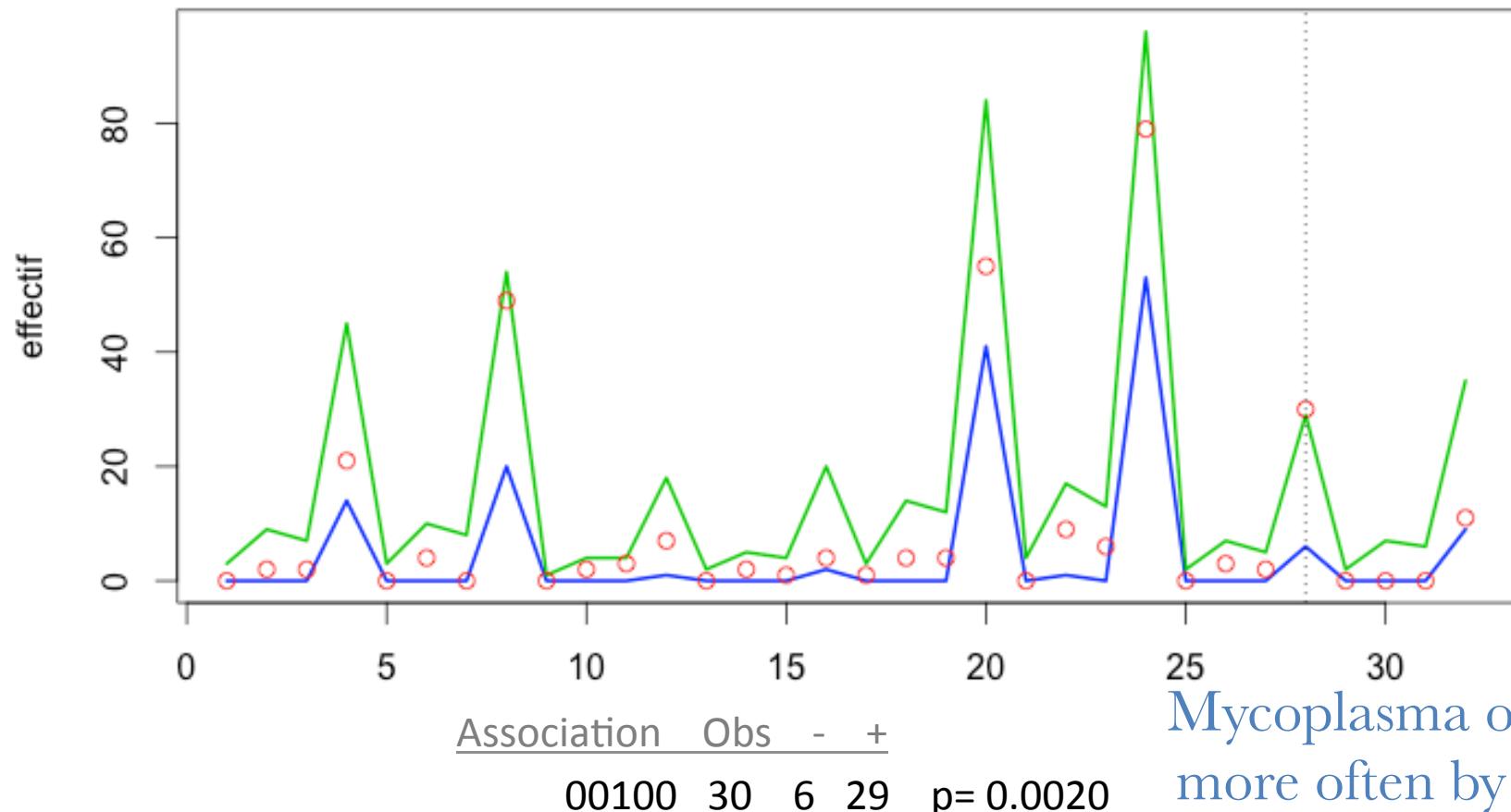


Screening Analysis



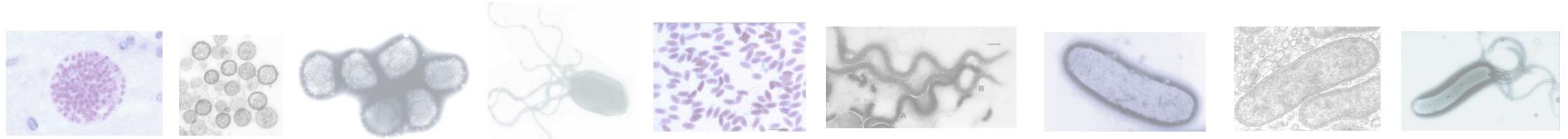


Screening Analysis

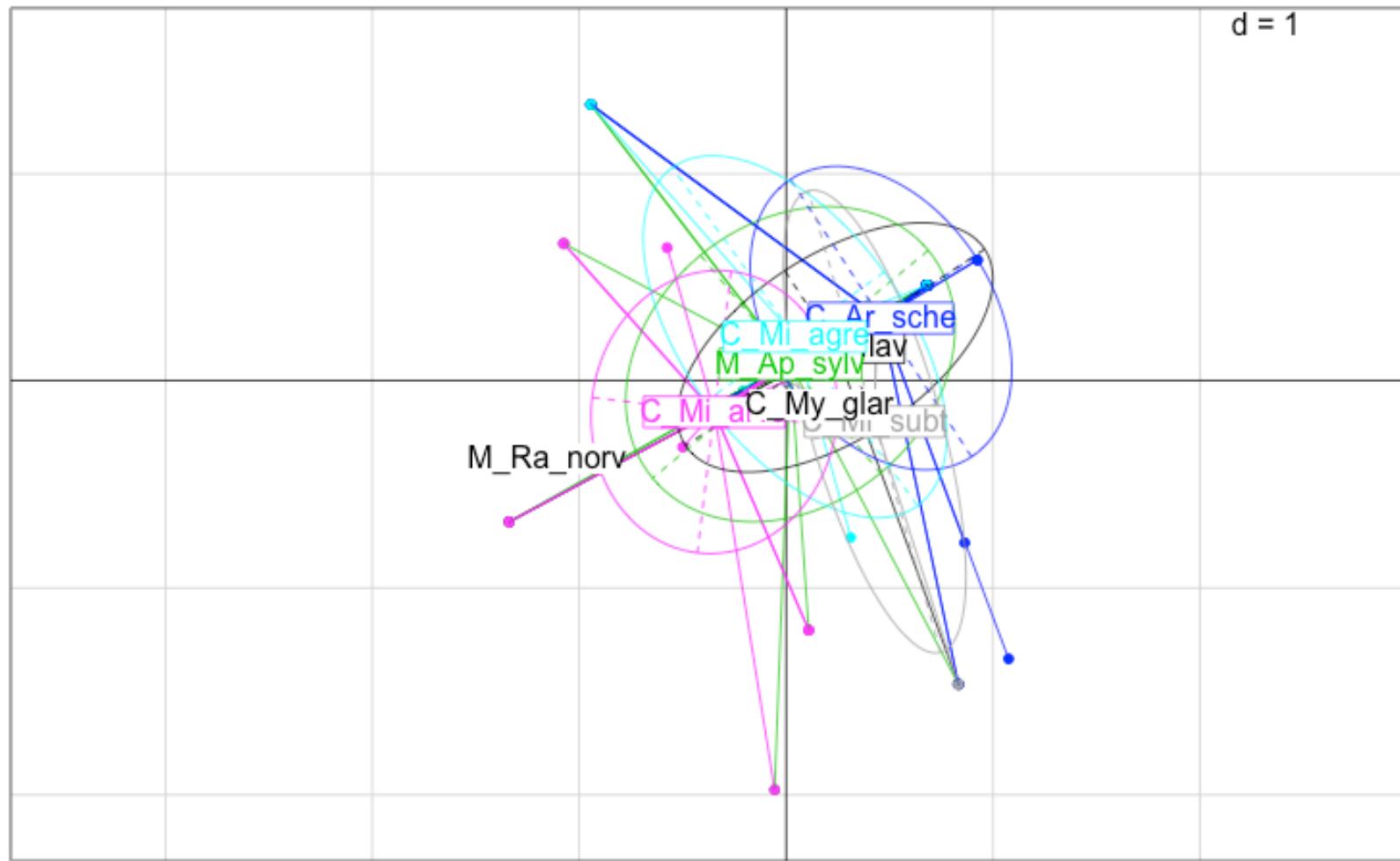


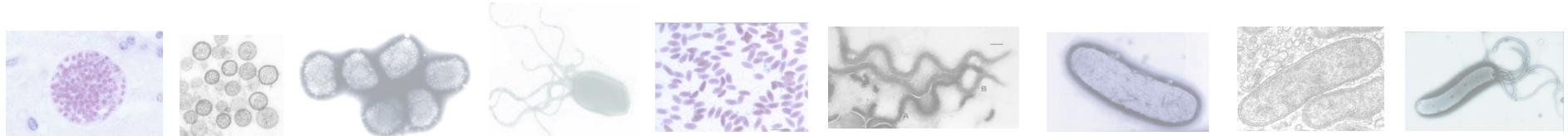
Mycoplasma occurs
more often by itself
than by chance





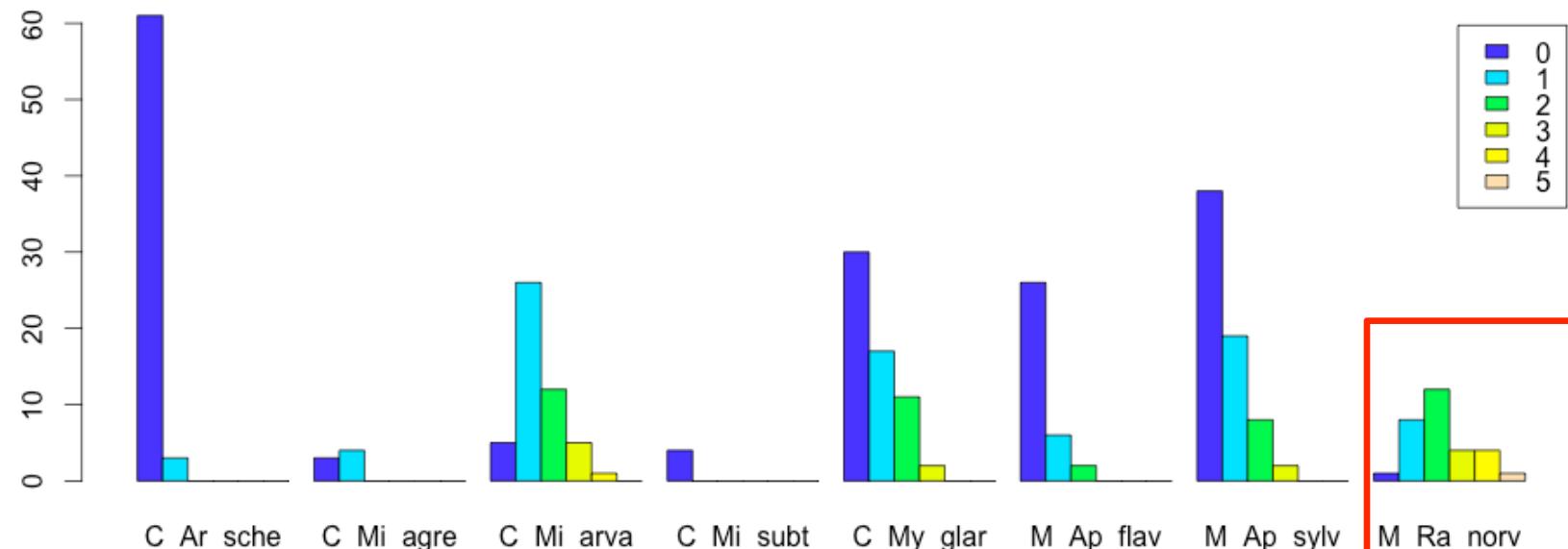
Screening Analysis

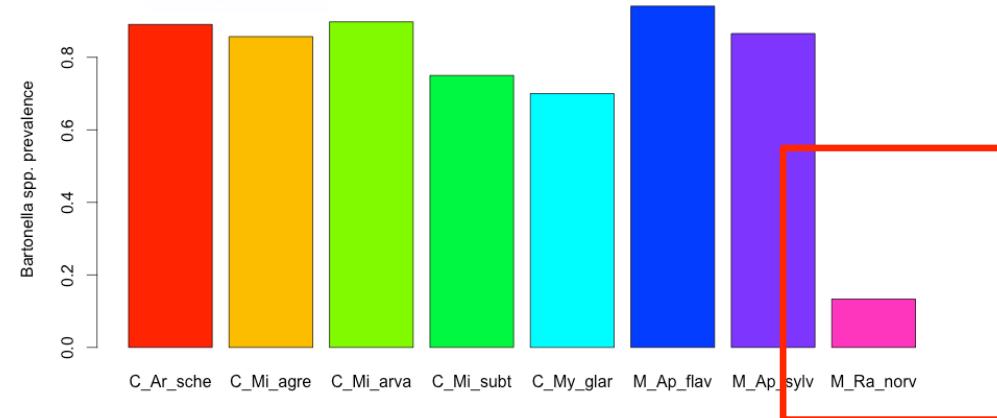
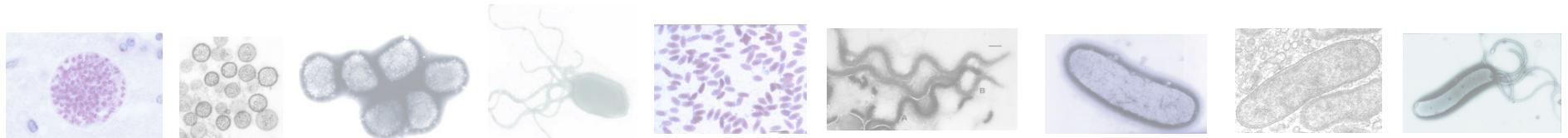




Screening Analysis

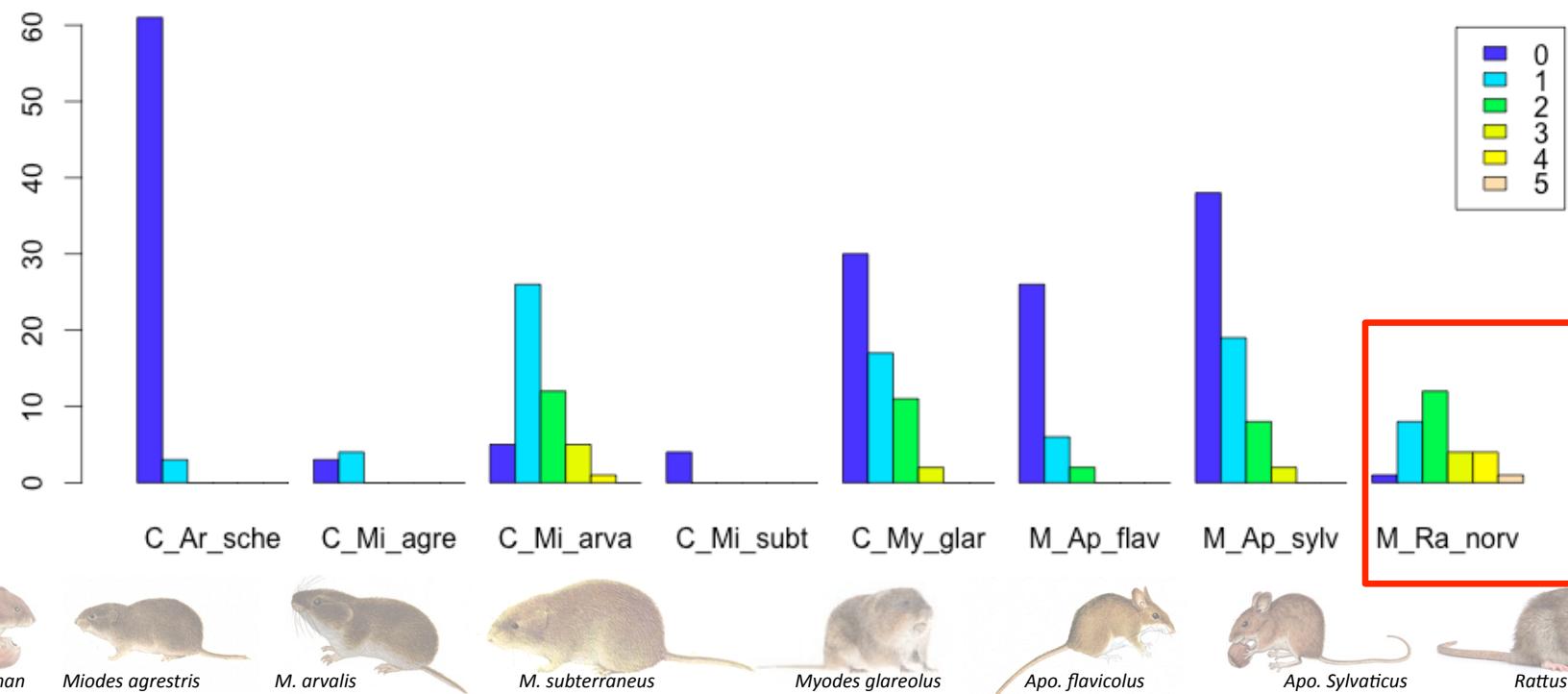
Number of Mycobacterium Species per Individual

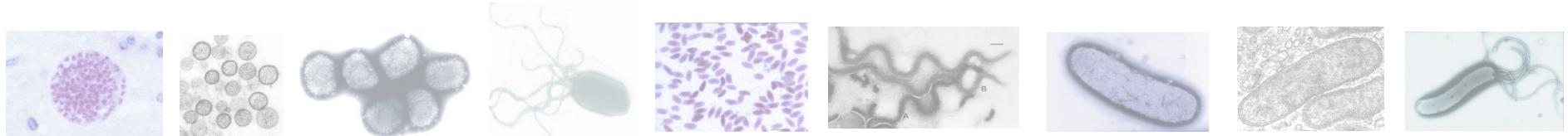




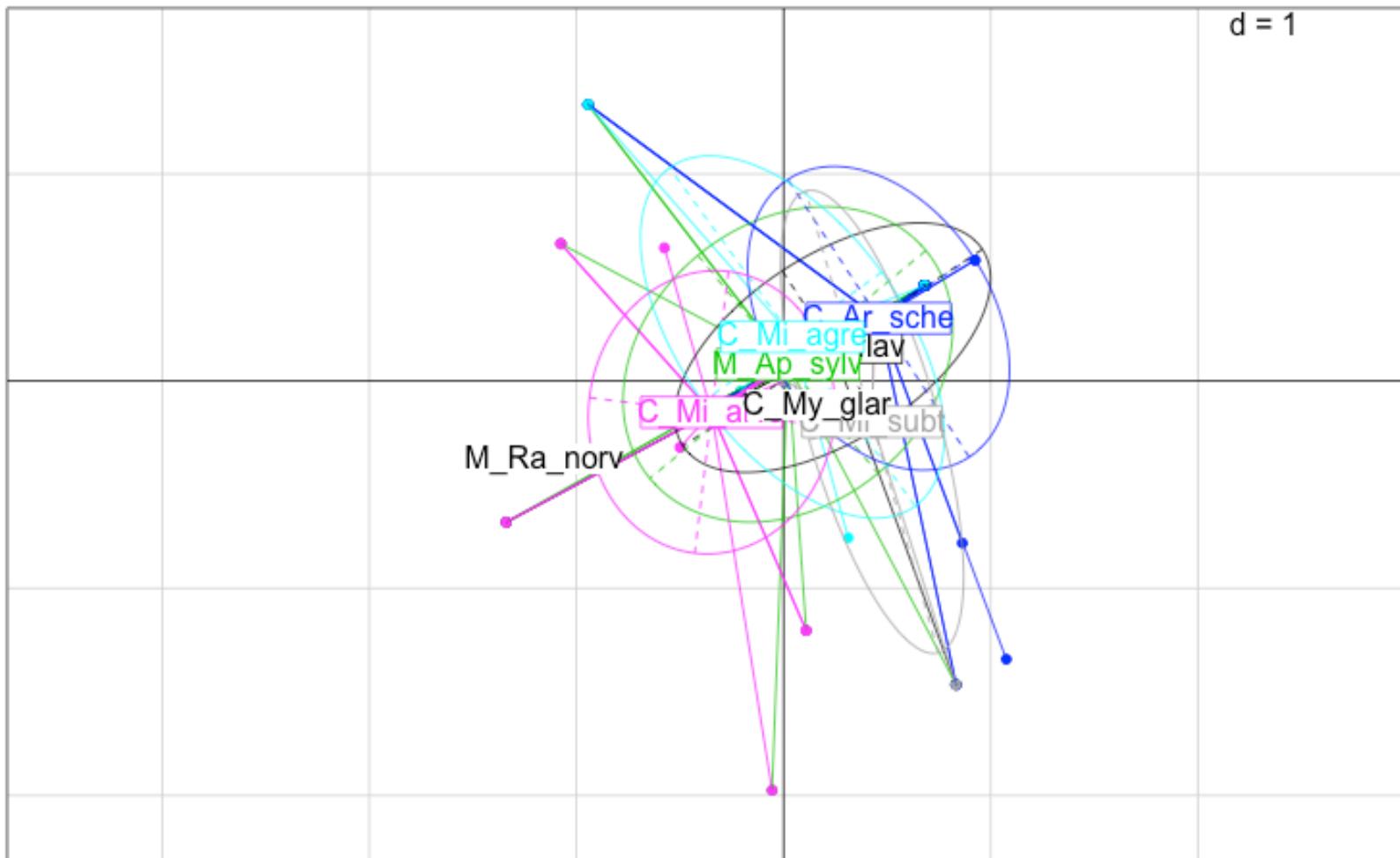
Bartonella spp.

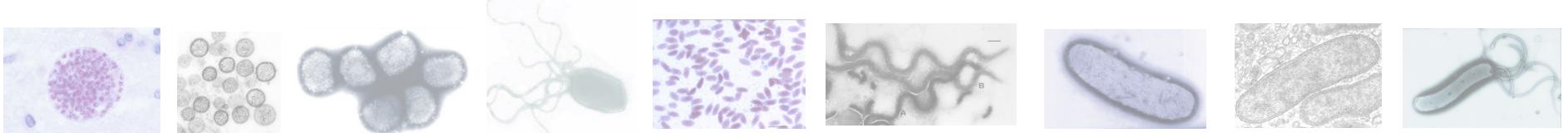
Number of Mycobacterium Species per Individual



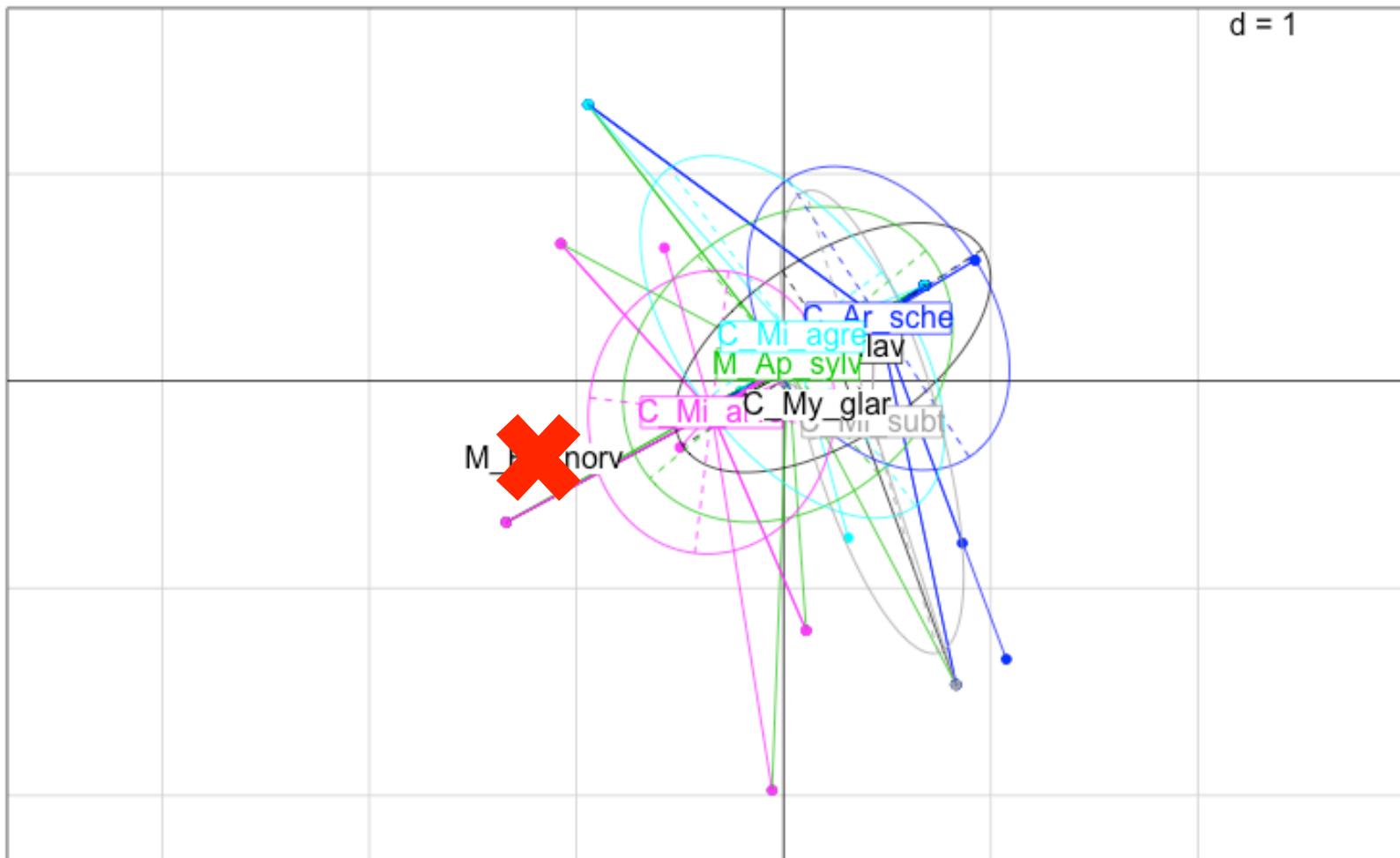


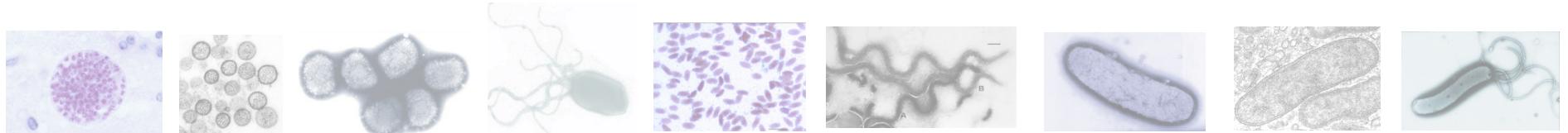
Screening Analysis



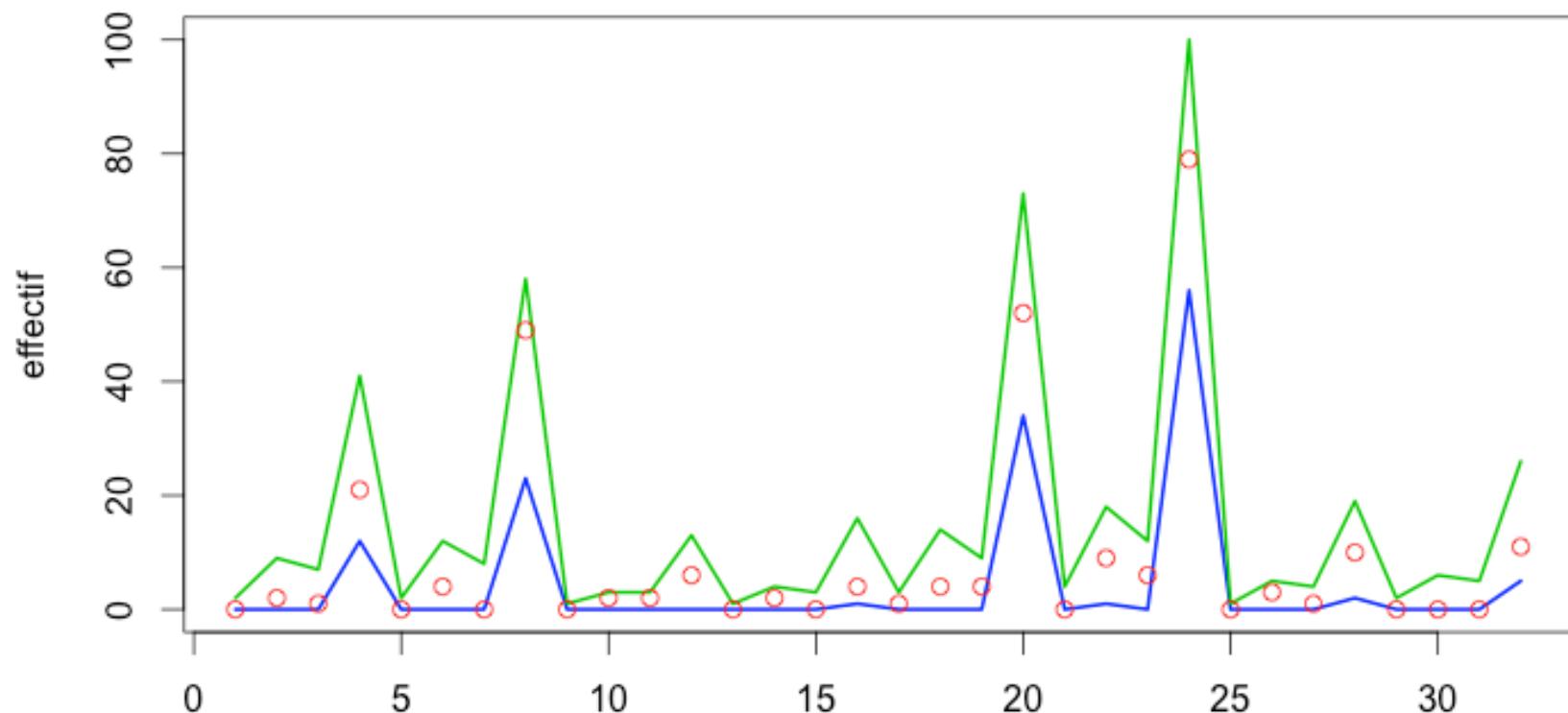


Screening Analysis





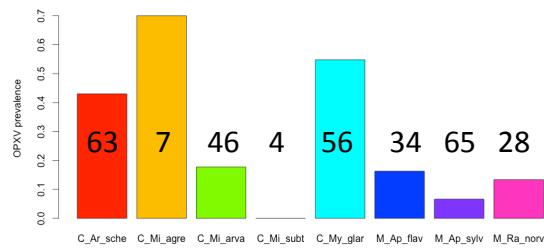
Screening Analysis



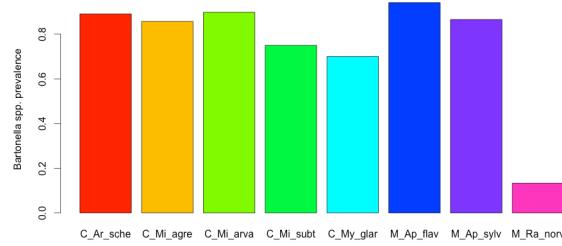
Mycoplasma occurs
more often than itself
than by chance



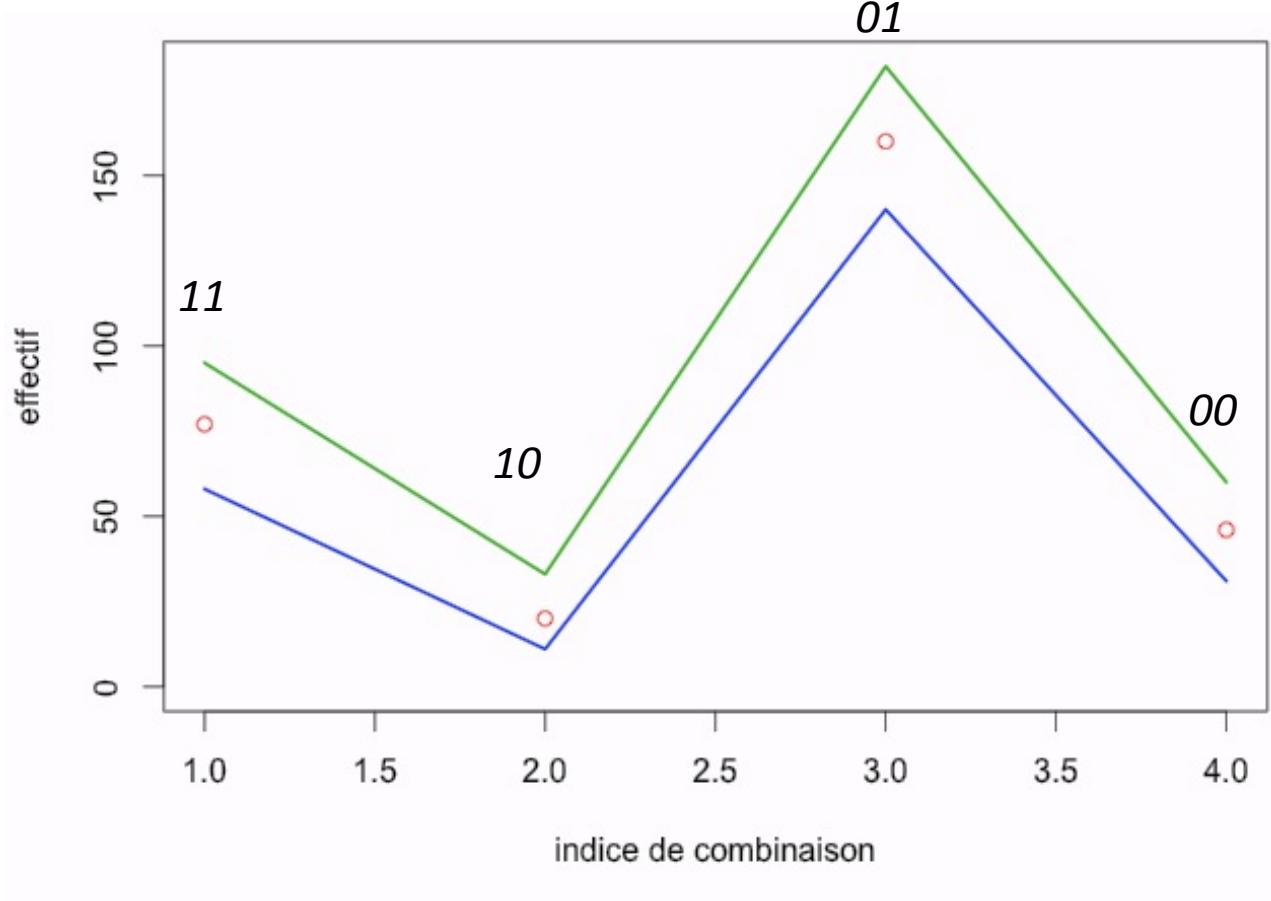
OPXV antibodies



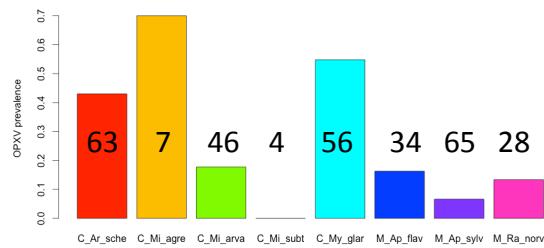
Overall *Bartnolla* spp. prevalence



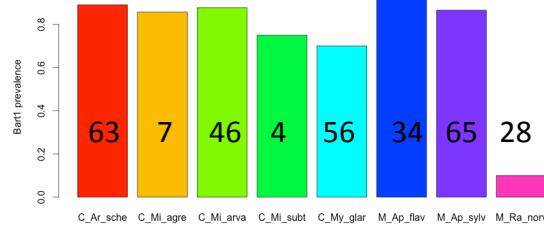
Screening Analysis



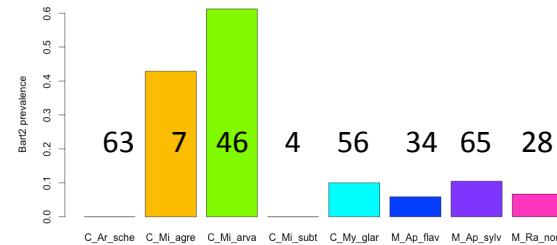
OPXV antibodies



Bartonella spp. 1



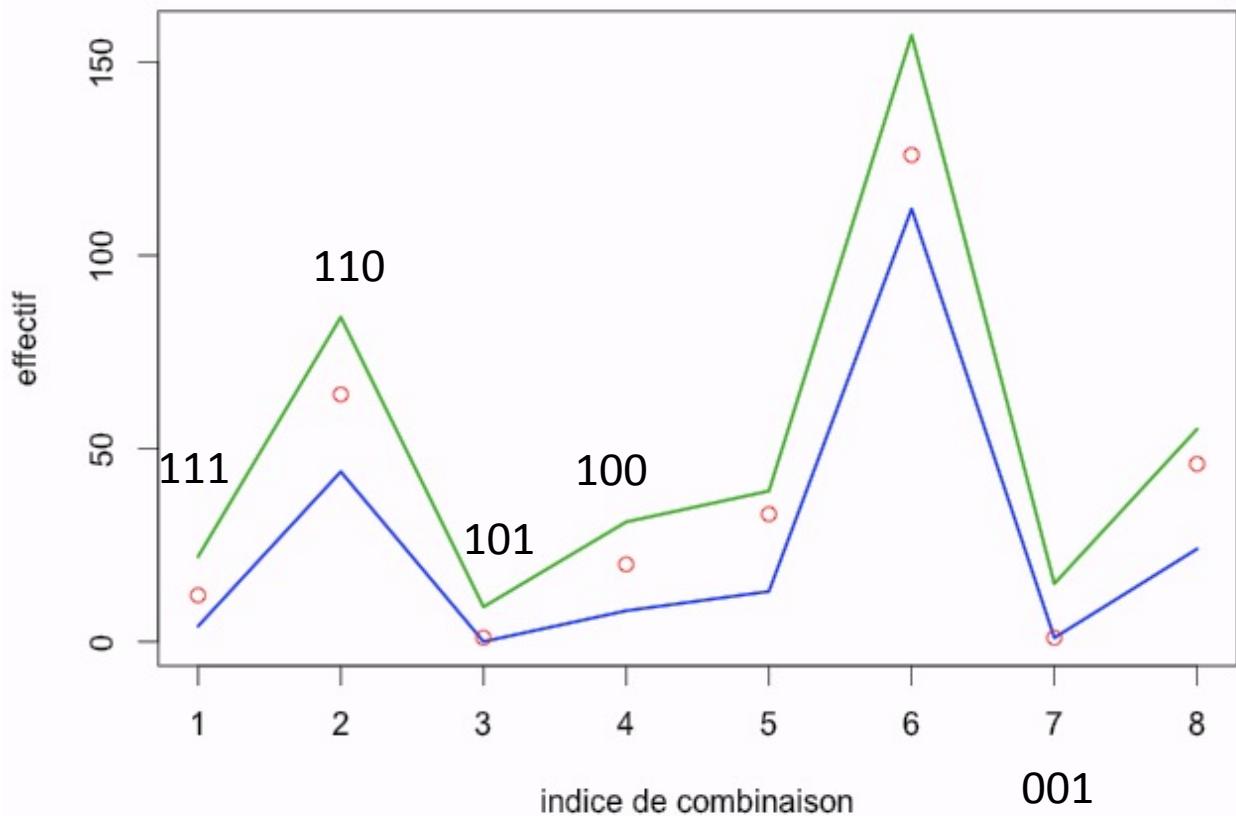
Bartonella spp. 2



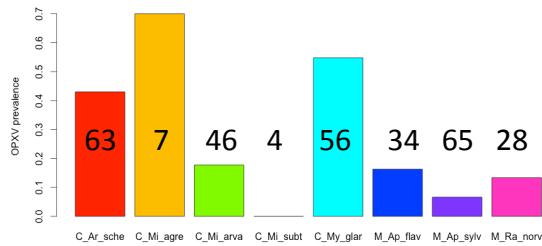
Screening Analysis

Association Obs - +

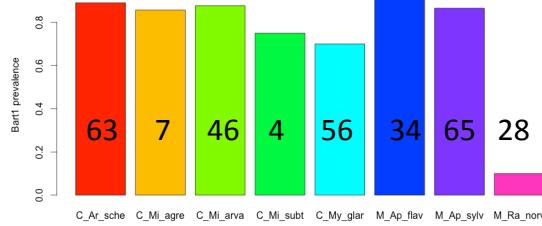
001 1 1 15 p = 0.0116



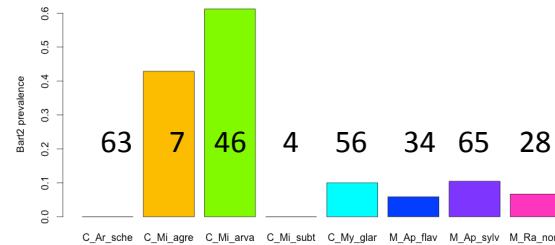
OPXV antibodies



Bartonella spp. 1



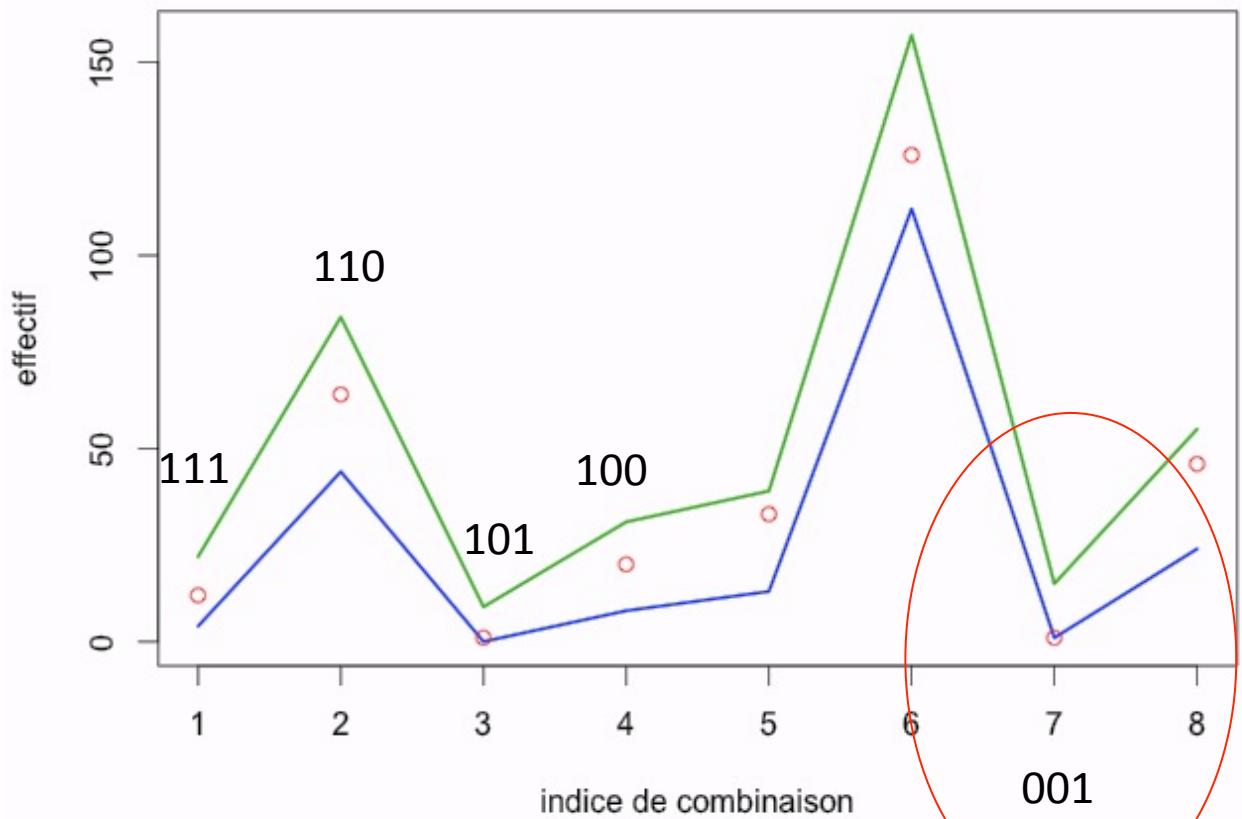
Bartonella spp. 2



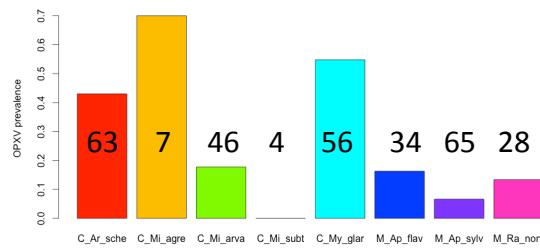
Screening Analysis

Association Obs - +

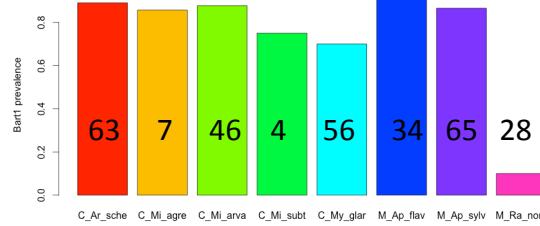
001 1 1 15 p = 0.0116



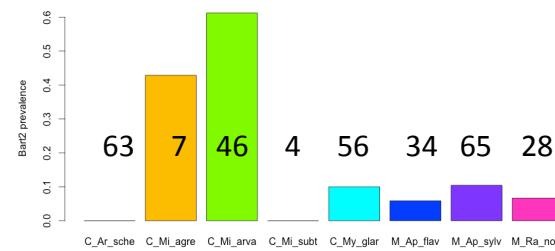
OPXV antibodies



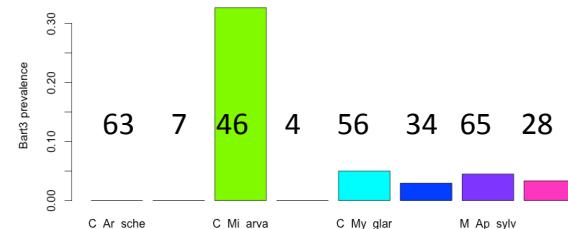
Bartonella spp. 1



Bartonella spp. 2



Bartonella spp. 3

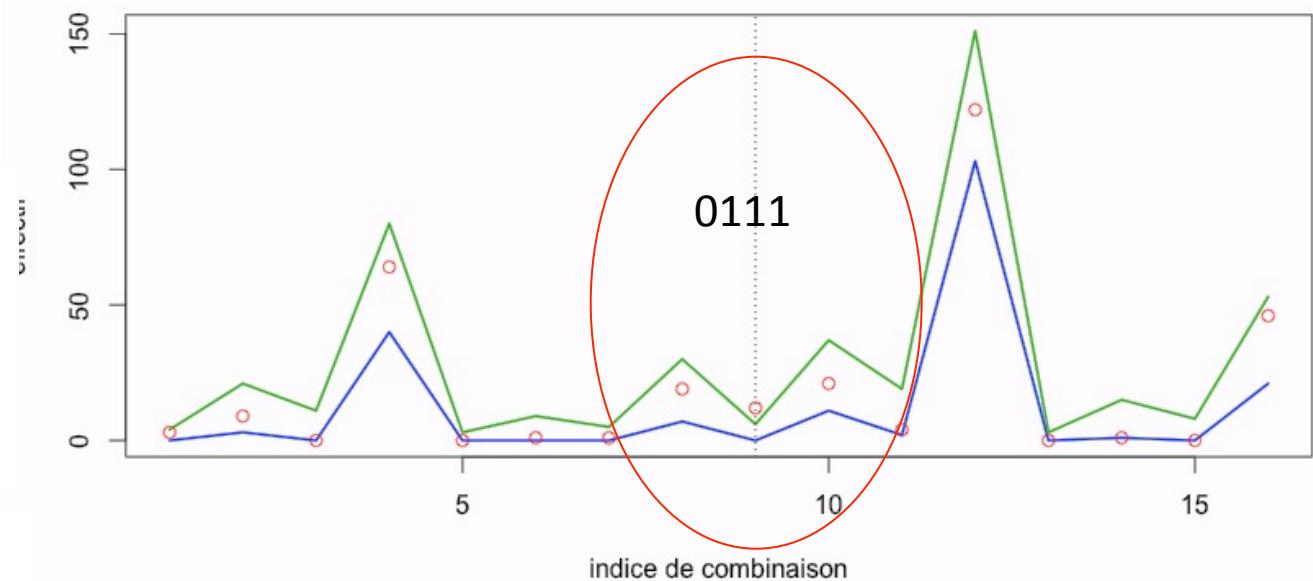


Screening Analysis

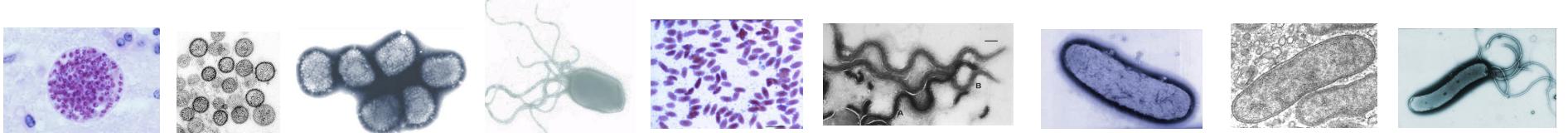
Association Obs - +

0111 12 0 6

p = 0



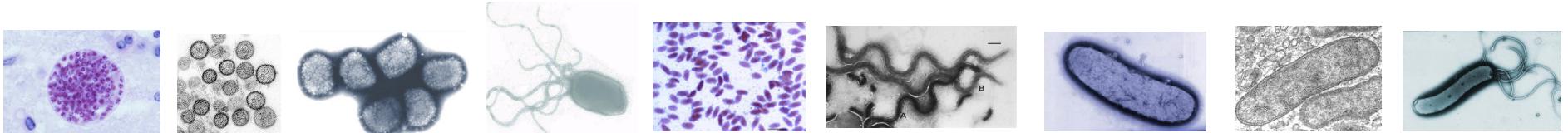
Negative association OPXV & Bartonella species richness?



Summary

- ✓ Do co-infections occur?
- ✓ What determines co-infection rates?
- ✗ Are there associations (+ & -) between parasites (or a history thereof)?

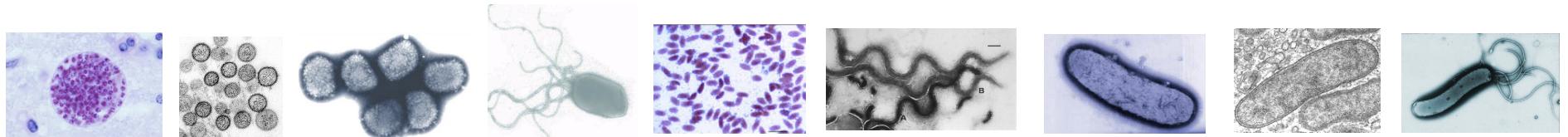




Perspectives

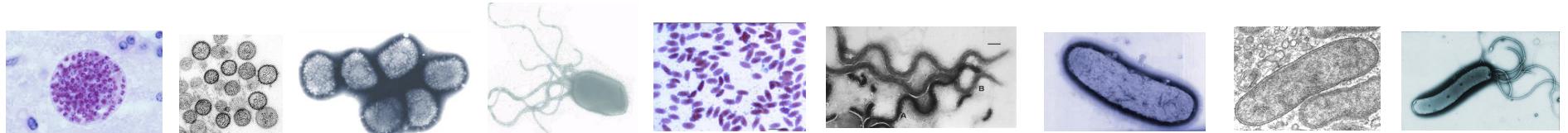
- How does OPXV affect the species-richness of the *pathobiome*?
- What about opportunistic infections of the splenic *microbiome*?
- How does *phylogenetic distance* impact the detection and/or reality of parasite-parasite interactions?





Thank you!





Bon retrait!



