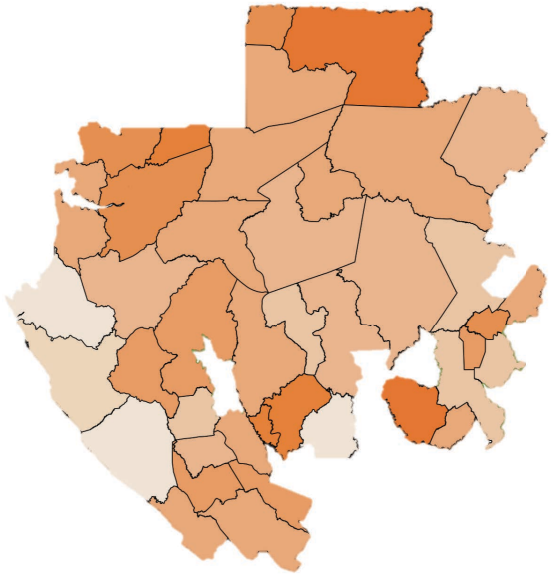
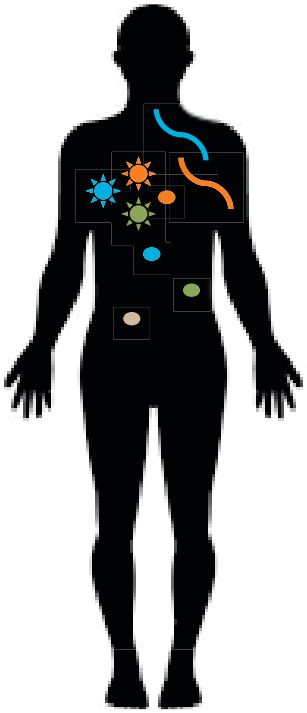
The human pathobiome: detection of pathogen-pathogen interactions from snapshot surveillance data





JESSICA L. ABBATE

Jessie.Abbate@gmail.com / IRD équipe SEE

½ Journée "Réseaux, Invasions et Emergences"

11 Mai 2017

❖ Août 2012
Thèse : Biologie
Univ. de Virginie, USA

Recherches post-doctorales

❖ 2012-2014
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❖ 2014-2015
INRA / UMR CBGP

❖ 2015
Université de Berne

❖ 2015-2017
UMMISCO / MIVEGEC

1. Déterminants de la Distribution et de la Sévérité des Maladies Infectieuses

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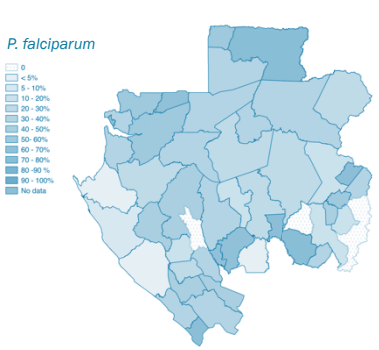
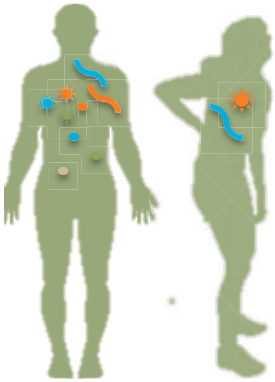
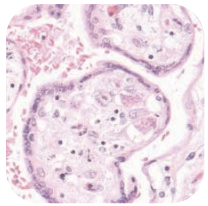
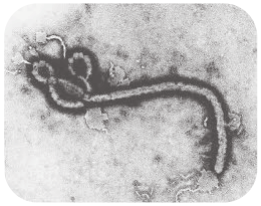
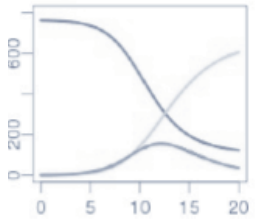




- Manips et Gestion de grands jeux de données
- Statistiques multifactorielles & computationelles
- Modélisation épidémiologique
- Intégration de données empiriques dans des modèles méchanistiques





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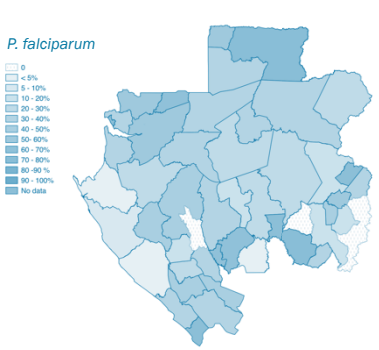

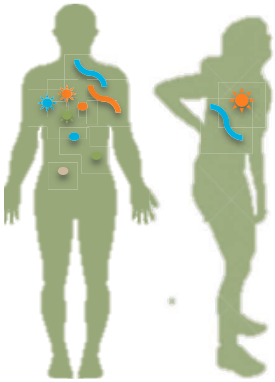

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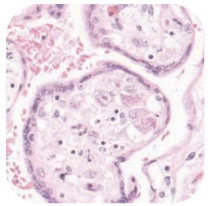
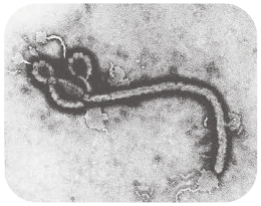
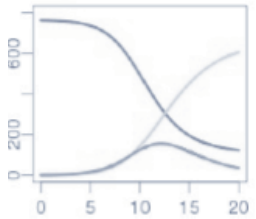
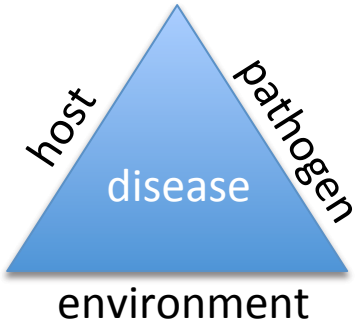
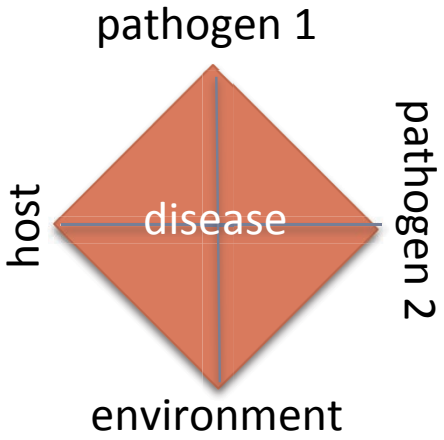
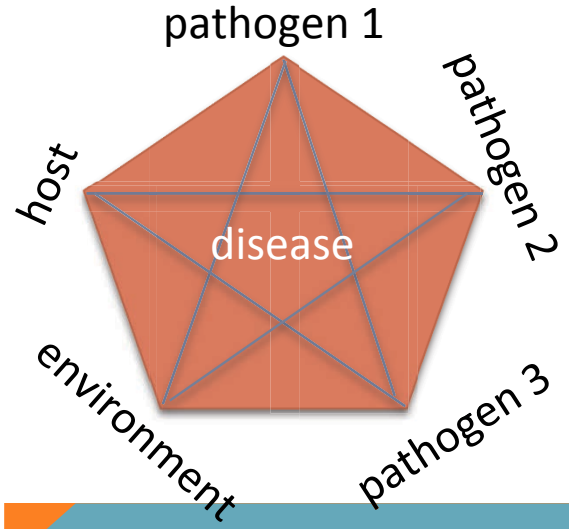


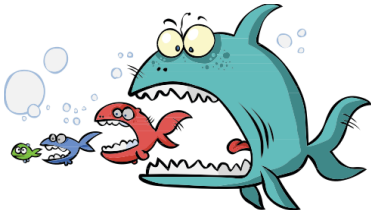


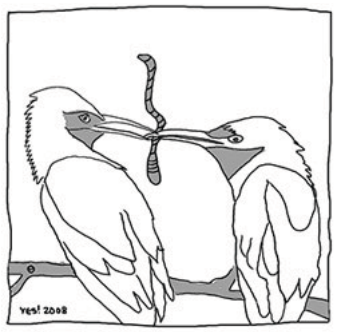



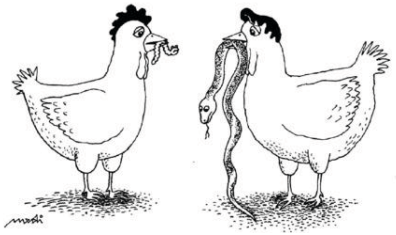


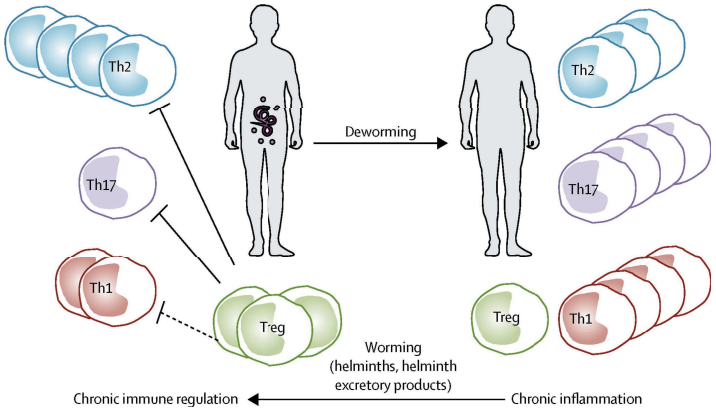






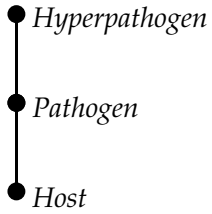




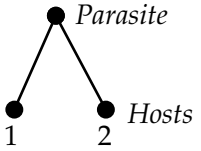


Community modules in epidemiology

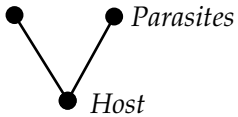
Parasite chain



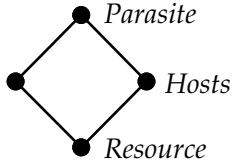
Shared parasitism



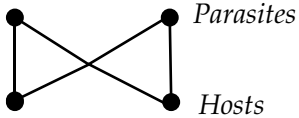
Parasite competition



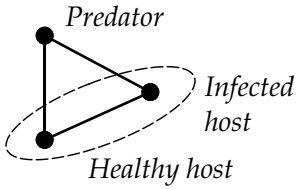
Keystone parasitism

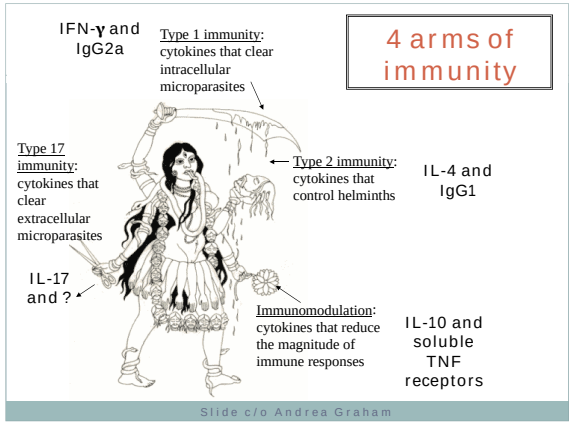


Niche partitioning



Predation on hosts





From understanding individual infections to understanding the impacts of the ‘pathobiome’ or ‘pathocenosis’.

How can we detect pathogen-pathogen interactions in humans (and other species) using minimally-invasive techniques?

- snapshot disease surveillance data (e.g., 16s, antibody screening, etc. on individuals at a single point in time)
- at least to generate novel hypotheses

Individu	LL	FP	MA	HCV	HTLV	EBO	RFT	DEN	WNV	CHK
662	1	0	1	0	0	1	0	0	1	1
663	0	1	1	0	0	1	0	0	0	0
664	0	1	1	0	0	0	0	0	1	0
665	0	0	0	0	0	0	0	0	0	0
666	0	0	0	0	0	0	0	0	0	0
667	0	0	0	0	0	0	0	0	1	0

❖ 2014-2015

INRA / UMR CBGP

Nathalie Charbonnel

Écologie et Évolution des Zoonoses

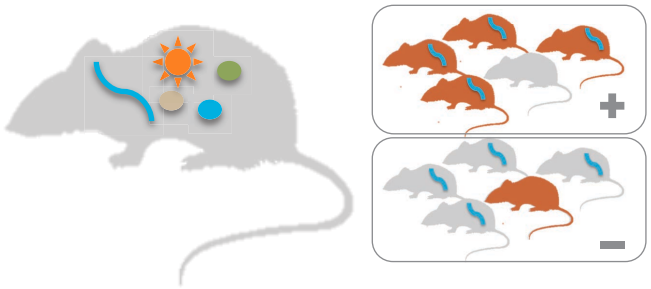
(Toxoplasmose, Immuno-écologie)

- Natural History & Population Dynamics
- Geographic Distribution & Evolutionary History
- Host – Pathogen Genetics
- Phenotype & Life-History Traits
- Environmental Variables
- **Ecological Interactions**

Explorer :

- l'impact du « pathobiome » sur la distribution de zoonoses chez les rongeurs sauvages

virus
protozoaires
helminthes
bactéries (NGS-16S)

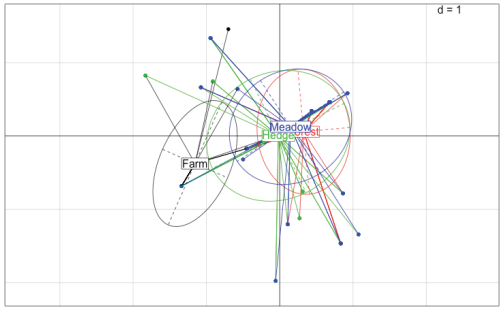


- Gestion et analyses de données NGS

700+ individus (cohorte)
20+ espèces de bactéries pathogènes (16S rRNA)

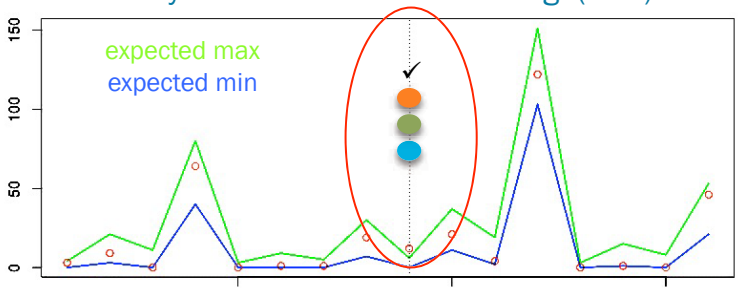
- Intégration des cofacteurs écologiques

Analyses des Correspondances Multiples



- Identification d'associations

Analyses d'*Association Screening* (**SCN**)



pour chaque combinaison possible de pathogènes

Vaumourin et al. 2014

❖ 2015-2017

UMMISCO / MIVEGEC

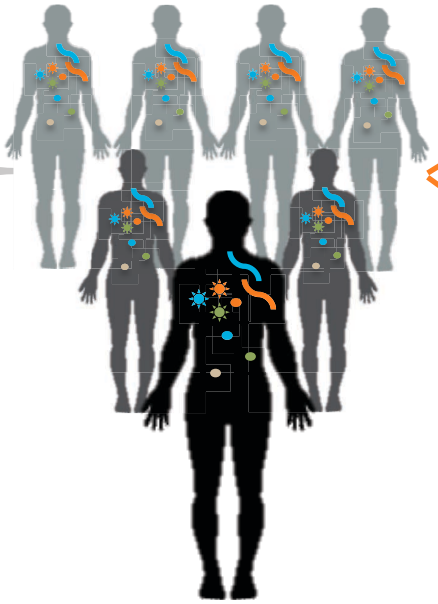
Benjamin Roche

Santé, Écologie & Évolution
(Diversité et Maladies Infectieuses)

- Natural History & Population Dynamics
- Geographic Distribution & Evolutionary History
- Host – Pathogen Genetics
- Phenotype & Life-History Traits
- Environmental Variables
- **Ecological Interactions**

Quantifier :

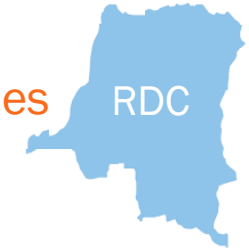
- l'impact des interactions inter-parasitaires sur la santé publique



- la prévalence des pathogènes?
- la sévérité des maladies?

Données de veille sanitaire chez l'homme

CIRMF
4200 volontaires
12 parasites
- helminthes
- virus
- *Plasmodium* spp. (NGS)

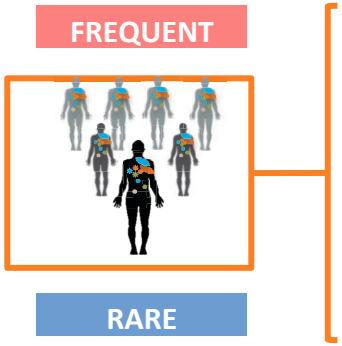


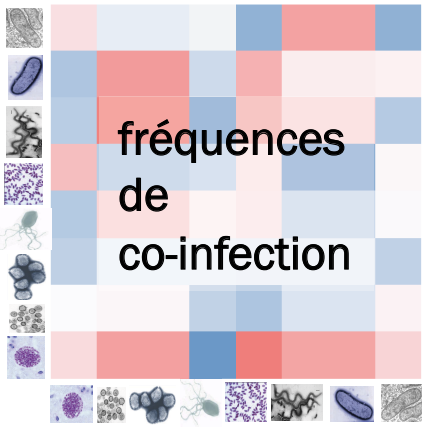
CUK
450 patients
7 Virus
- 5 Hepatites
- 3 Arbovirus

(INSERM-CIC)
280 patients
- *P. falciparum* infection & sévérité
- 5 helminthes

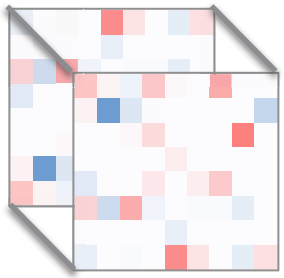
How can we detect pathogen-pathogen interactions in humans (and other species) using minimally-invasive techniques?

- snapshot disease surveillance data (e.g., 16s, antibody screening, etc. on individuals at a single point in time)





Interactions multidimensionnelles :



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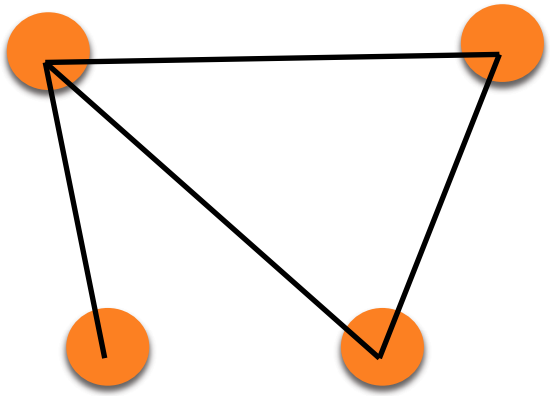
Association Screening Analysis
(Vaumourin *et al.*, 2014)



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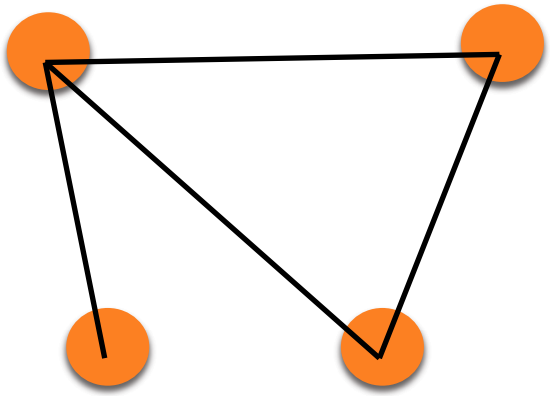

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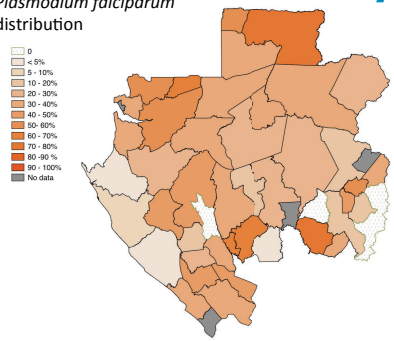
666	0	0	0	0	0	0	0	0	0	0
667	0	0	0	0	0	0	0	0	1	0

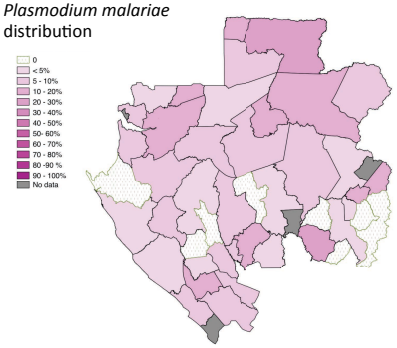
2^N combinations (coinfection statuses)
→ table of coinfection status frequencies

Association Screening Analysis (Vaumourin et al. 2014)

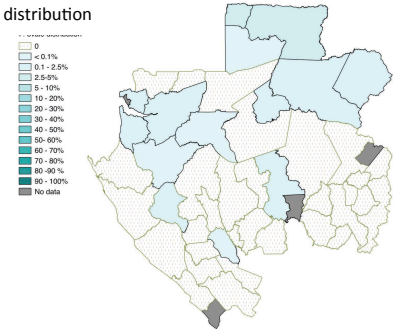
Plasmodium falciparum distribution



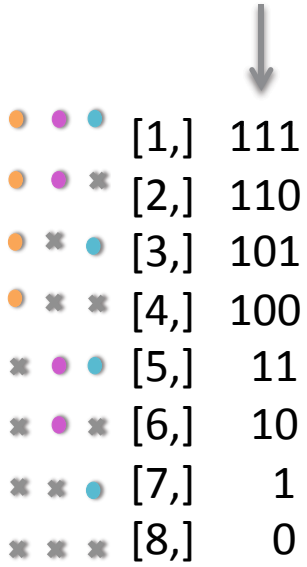
Plasmodium malariae distribution



Plasmodium ovale distribution



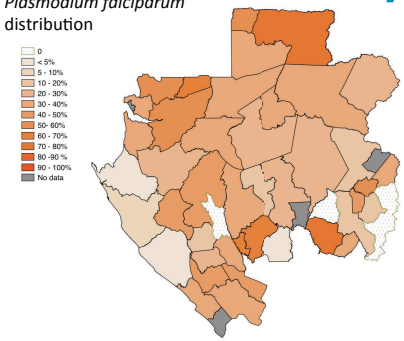
Pf, Pm, Po



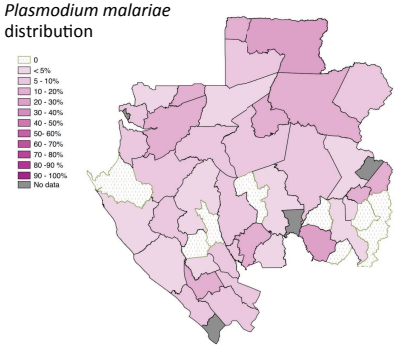
[1,]	111
[2,]	110
[3,]	101
[4,]	100
[5,]	11
[6,]	10
[7,]	1
[8,]	0

Association Screening Analysis (Vaumourin et al. 2014)

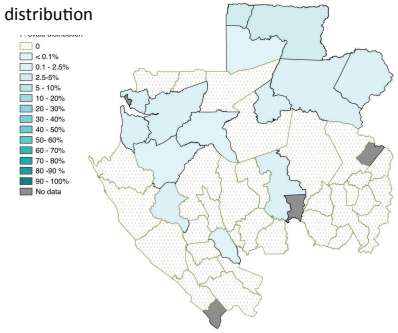
Plasmodium falciparum distribution



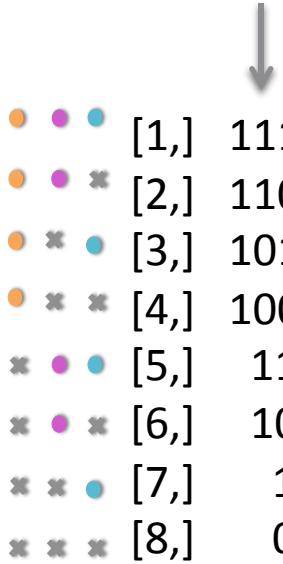
Plasmodium malariae distribution



Plasmodium ovale distribution



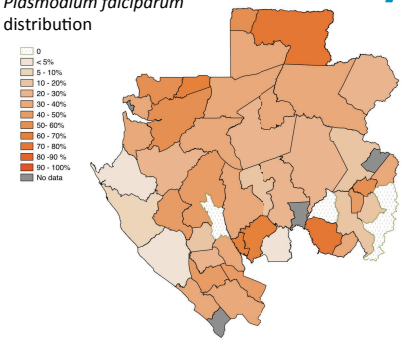
Pf, Pm, Po



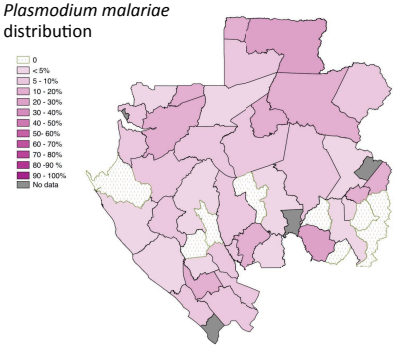
		-	+
[1,]	111	0	5
[2,]	110	99	158
[3,]	101	4	22
[4,]	100	1297	1466
[5,]	11	0	7
[6,]	10	192	270
[7,]	1	10	34
[8,]	0	2422	2592

Association Screening Analysis (Vaumourin et al. 2014)

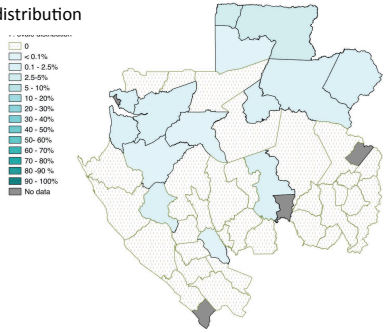
Plasmodium falciparum distribution

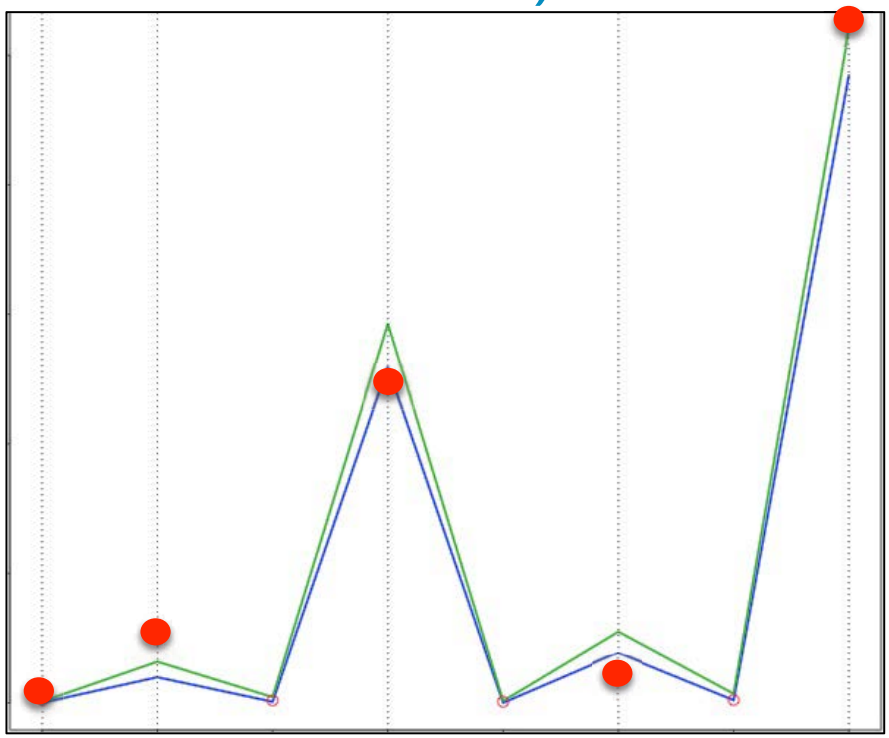


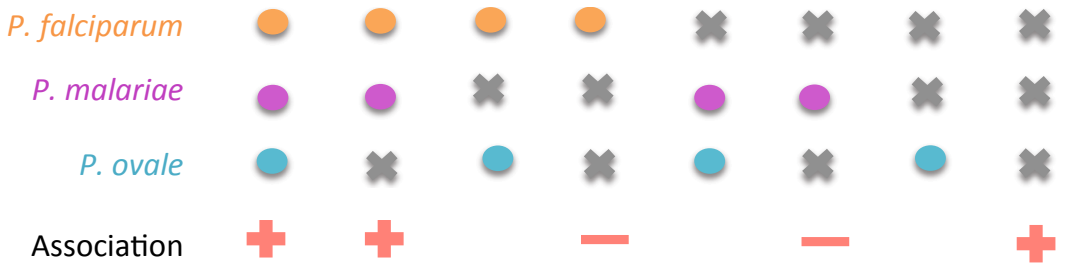
Plasmodium malariae distribution



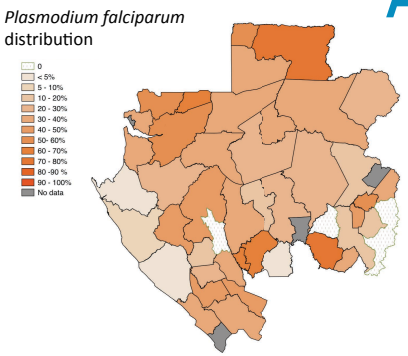
Plasmodium ovale distribution

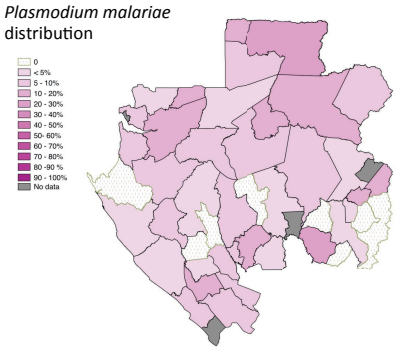


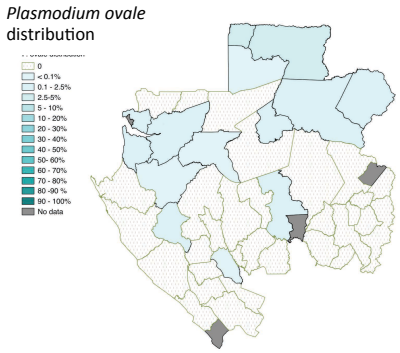




Association Screening Analysis (Vaumourin et al. 2014)



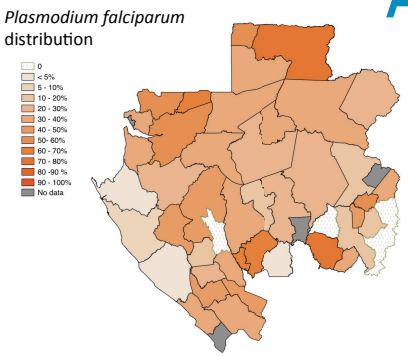


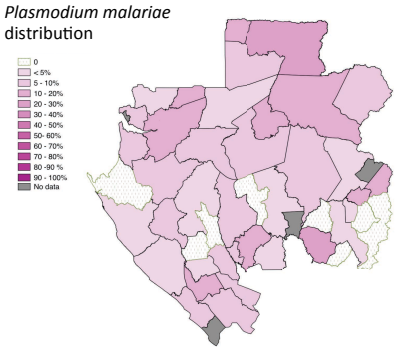


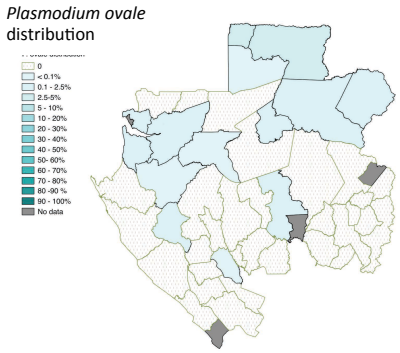
Pf, Pm, Po

	Obs.	-	+	sig?	p
[1,]	111	12	0	5	1	0.0000
[2,]	110	243	99	158	1	0.0000
[3,]	101	9	4	22	0	0.5464
[4,]	100	1256	1297	1466	1	0.0000
[5,]	11	4	0	7	0	0.2780
[6,]	10	103	192	270	1	0.0000
[7,]	1	11	10	34	0	0.0212
[8,]	0	2645	2422	2592	1	0.0000

Association Screening Analysis (Vaumourin et al. 2014)







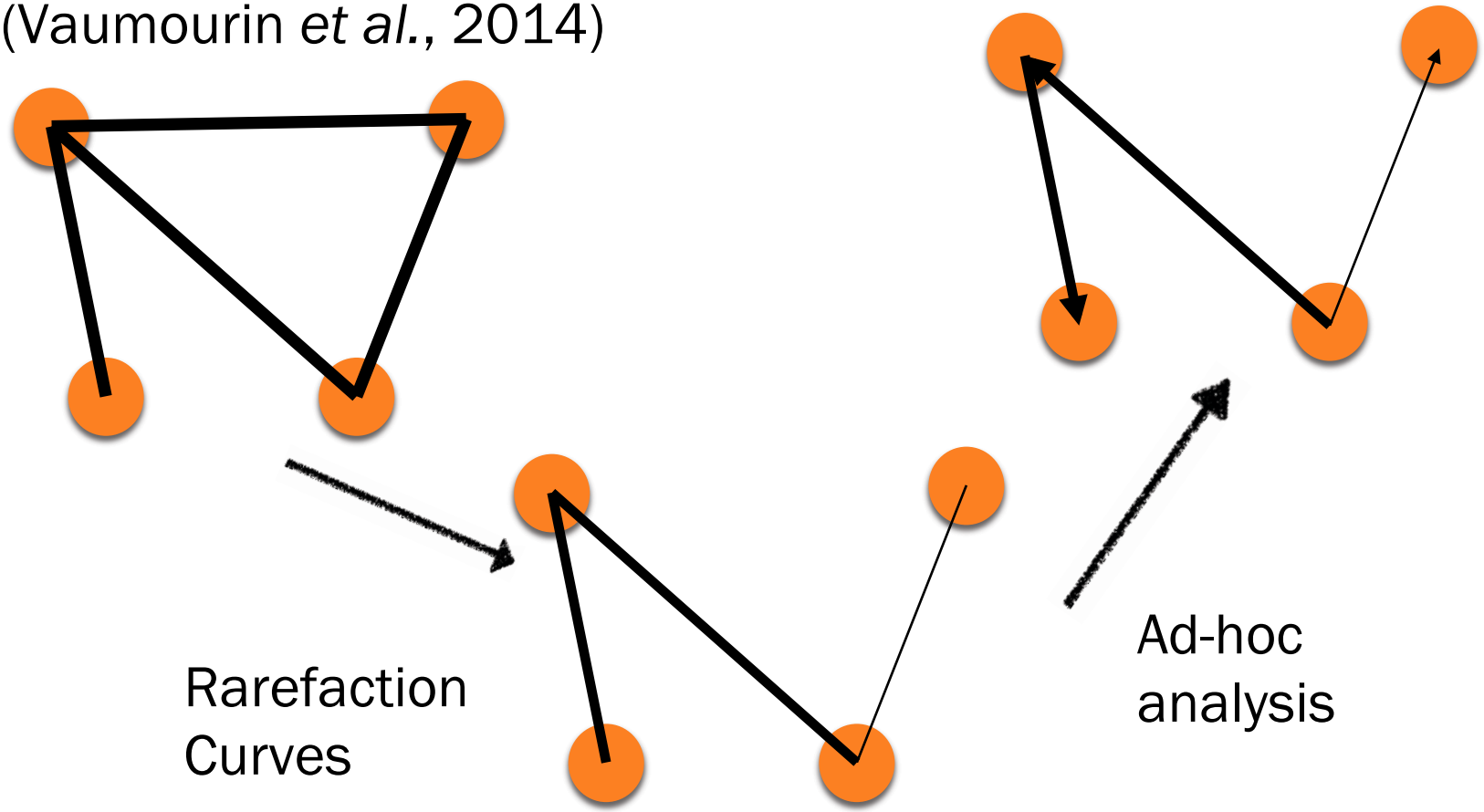
Pf, Pm, Po

		Obs.	-	+	sig?	p
● ● ●	[1,]	111	12	0	5	1	0.0000
● ● ✖	[2,]	110	243	99	158	1	0.0000
● ✖ ●	[3,]	101	9	4	22	0	0.5464
● ✖ ✖	[4,]	100	1256	1297	1466	1	0.0000
✖ ● ●	[5,]	11	4	0	7	0	0.2780
✖ ● ✖	[6,]	10	103	192	270	1	0.0000
✖ ✖ ●	[7,]	1	11	10	34	0	0.0212
✖ ✖ ✖	[8,]	0	2645	2422	2592	1	0.0000

How can we detect pathogen-pathogen interactions in humans (and other species) using minimally-invasive techniques?

- snapshot disease surveillance data (e.g., 16s, antibody screening, etc. on individuals at a single point in time)

Association Screening Analysis
(Vaumourin *et al.*, 2014)



SCN + Rarefaction

Association:	ll	fp	ma	hc	ht	eb	rf	de	wn	ch			% data sampled									robustness
Order	ll	fp	ma	hc	ht	eb	rf	de	wn	ch	As	Direction	10%					→			100%	score (RR)
1018								1	1	0	#	Frequent	0	0	0	0	0	1	1	1	1	5
880			1	0	0	1	0	0	0	0	#	Frequent	0	0	0	0	0	0	1	1	1	4
1017								1	1	1	#	Frequent	0	0	0	0	0	0	1	1	1	4
1014							1	0	1	0	#	Frequent	0	0	0	0	0	0	0	1	1	3
112	1	1	1	0	0	1	0	0	0	0	#	Frequent	0	0	0	0	0	0	0	1	1	3
892			1	0	0	0	0	1	0	0	#	Rare	0	0	0	0	0	0	0	0	1	2
1020								1	0	0	#	Rare	0	0	0	0	0	0	0	0	1	2
256	1	1	0	0	0	0	0	0	0	0	#	Frequent	0	0	0	0	0	0	0	0	1	2
830			1	1	0	0	0	0	1	0	#	Rare	0	0	0	0	0	0	0	0	1	2
505	1	0	0	0	0	0	0	1	1	1	#	Random	0	0	0	0	0	0	0	0	0	1
506	1	0	0	0	0	0	0	1	1	0	#	Frequent	0	0	0	0	0	0	0	0	0	1
126	1	1	1	0	0	0	0	0	1	0	#	Frequent	0	0	0	0	0	0	0	0	0	1
182	1	1	0	1	0	0	1	0	1	0	#	Random	0	0	0	0	0	0	0	0	0	1
298	1	0	1	1	0	1	0	1	1	0	#	Random	0	0	0	0	0	0	0	0	0	1
312	1	0	1	1	0	0	1	0	0	0	#	Random	0	0	0	0	0	0	0	0	0	1
1016							1	0	0	0	#	Rare	0	0	0	0	0	0	0	0	0	1
352	1	0	1	0	1	0	0	0	0	0	#	Frequent	0	0	0	0	0	0	0	0	0	1
415	1	0	0	1	1	0	0	0	0	1	#	Random	0	0	0	0	0	0	0	0	0	1
757		1	0	0	0	0	1	0	1	1	#	Random	0	0	0	0	0	0	0	0	0	1
489	1	0	0	0	0	1	0	1	1	1	#	Random	0	0	0	0	0	0	0	0	0	0
695		1	0	1	0	0	1	0	0	1	#	Random	0	0	0	0	0	0	0	0	0	0
469	1	0	0	0	1	0	1	0	1	1	#	Random	0	0	0	0	0	0	0	0	0	0
480	1	0	0	0	1	0	0	0	0	0	#	Frequent	0	0	0	0	0	0	0	0	0	0
633		1	1	0	0	0	0	1	1	1	#	Random	0	0	0	0	0	0	0	0	0	0
496	1	0	0	0	0	1	0	0	0	0	#	Rare	0	0	0	0	0	0	0	0	0	0
512	1	0	0	0	0	0	0	0	0	0	#	Rare	0	0	0	0	0	0	0	0	0	0

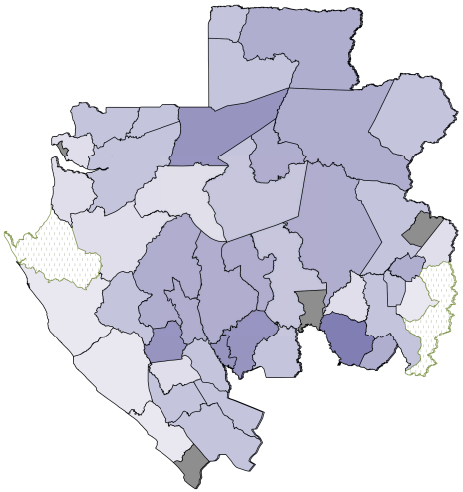
SCN + Rarefaction

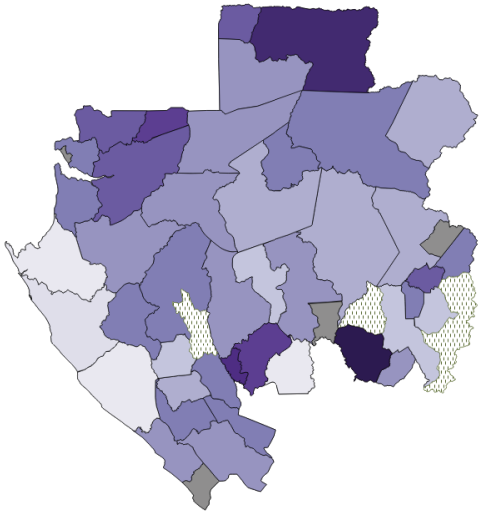
Association:	ll	fp	ma	hc	ht	eb	rf	de	wn	ch			% data sampled										robustness
Order	ll	fp	ma	hc	ht	eb	rf	de	wn	ch	As	Direction	10%					→				100%	score (RR)
1018								1	1	0	#	Frequent	0	0	0	0	0	1	1	1	1	1	5
880			1	0	0	1	0	0	0	0	#	Frequent	0	0	0	0	0	0	1	1	1	1	4
1017								1	1	1	#	Frequent	0	0	0	0	0	0	1	1	1	1	4
1014							1	0	1	0	#	Frequent	0	0	0	0	0	0	0	1	1	1	3
112	1	1	1	0	0	1	0	0	0	0	#	Frequent	0	0	0	0	0	0	0	1	1	1	3
892			1	0	0	0	0	1	0	0	#	Rare	0	0	0	0	0	0	0	0	1	1	2
1020								1	0	0	#	Rare	0	0	0	0	0	0	0	0	1	1	2
256	1	1	0	0	0	0	0	0	0	0	#	Frequent	0	0	0	0	0	0	0	0	1	1	2
830			1	1	0	0	0	0	1	0	#	Rare	0	0	0	0	0	0	0	0	1	1	2
505	1	0	0	0	0	0	0	1	1	1	#	Random	0	0	0	0	0	0	0	0	0	1	1
506	1	0	0	0	0	0	0	1	1	0	#	Frequent	0	0	0	0	0	0	0	0	0	1	1
126	1	1	1	0	0	0	0	0	1	0	#	Frequent	0	0	0	0	0	0	0	0	0	1	1
182	1	1	0	1	0	0	1	0	1	0	#	Random	0	0	0	0	0	0	0	0	0	1	1
298	1	0	1	1	0	1	0	1	1	0	#	Random	0	0	0	0	0	0	0	0	0	1	1
312	1	0	1	1	0	0	1	0	0	0	#	Random	0	0	0	0	0	0	0	0	0	1	1
1016							1	0	0	0	#	Rare	0	0	0	0	0	0	0	0	0	1	1
352	1	0	1	0	1	0	0	0	0	0	#	Frequent	0	0	0	0	0	0	0	0	0	1	1
415	1	0	0	1	1	0	0	0	0	1	#	Random	0	0	0	0	0	0	0	0	0	1	1
757		1	0	0	0	0	1	0	1	1	#	Random	0	0	0	0	0	0	0	0	0	1	1
489	1	0	0	0	0	1	0	1	1	1	#	Random	0	0	0	0	0	0	0	0	0	0	0
695		1	0	1	0	0	1	0	0	1	#	Random	0	0	0	0	0	0	0	0	0	0	0
469	1	0	0	0	1	0	1	0	1	1	#	Random	0	0	0	0	0	0	0	0	0	0	0
480	1	0	0	0	1	0	0	0	0	0	#	Frequent	0	0	0	0	0	0	0	0	0	0	0
633		1	1	0	0	0	0	1	1	1	#	Random	0	0	0	0	0	0	0	0	0	0	0
496	1	0	0	0	0	1	0	0	0	0	#	Rare	0	0	0	0	0	0	0	0	0	0	0
512	1	0	0	0	0	0	0	0	0	0	#	Rare	0	0	0	0	0	0	0	0	0	0	0

Gabon Results

Ebola Ab

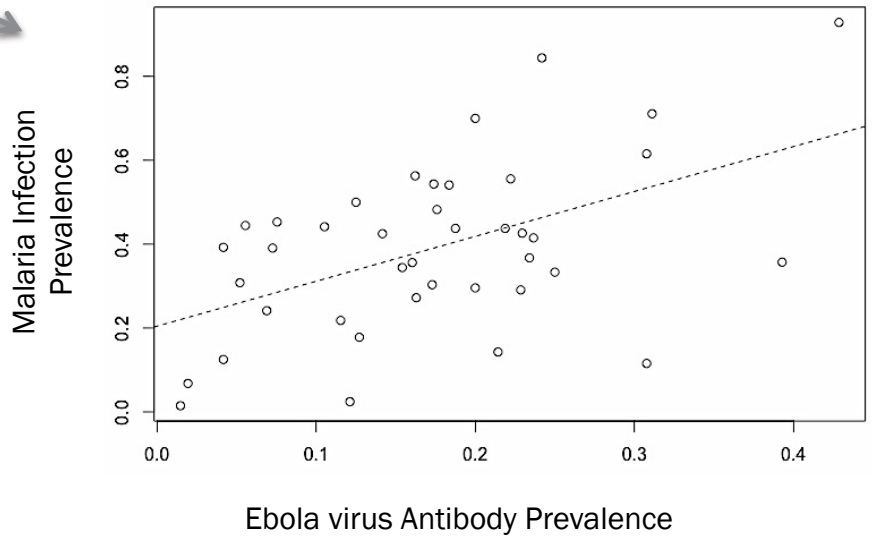
Malaria Infection





Interesting patterns identified:

1. Chicken or the egg: Geographic distributions for malaria infection and Ebola virus antibodies are tightly correlated ($\rho=0.43$, $p<0.01$)



Gabon Results

Interesting patterns identified:

3. Chicken or the egg: Geographic distributions for malaria infection and Ebola virus antibodies are tightly correlated (ρ=0.43, p<0.01), but the positive association remains significant even after this has been taken into account (GLMM).

SCN + Rarefaction

Association:	ll	fp	ma	hc	ht	eb	rf	de	wn	ch			% data sampled 10% → 100%									robustness score
Order	ll	fp	ma	hc	ht	eb	rf	de	wn	ch	As	Direction										
1018								1	1	0	#	Frequent	0	0	0	0	0	1	1	1	1	5
880			1	0	0	1	0	0	0	0	#	Frequent	0	0	0	0	0	0	1	1	1	4
1017								1	1	1	#	Frequent	0	0	0	0	0	0	1	1	1	4
1014							1	0	1	0	#	Frequent	0	0	0	0	0	0	0	1	1	3
112	1	1	1	0	0	1	0	0	0	0	#	Frequent	0	0	0	0	0	0	0	1	1	3
892			1	0	0	0	0	1	0	0	#	Rare	0	0	0	0	0	0	0	0	1	1	2
1020								1	0	0	#	Rare	0	0	0	0	0	0	0	0	1	1	2
256	1	1	0	0	0	0	0	0	0	0	#	Frequent	0	0	0	0	0	0	0	0	1	1	2
830			1	1	0	0	0	0	1	0	#	Rare	0	0	0	0	0	0	0	0	1	1	2

Response: **Probability of *Plasmodium* spp. Infection**

Random effects:

Groups	Name	Variance	Std.Dev.
Department	(Intercept)	0.9276	0.9631

Number of obs: 4091 , 40 department groups

Fixed effects:

	Estimate	Std. Error	z value	Pr(>|z|)	
(Intercept)	-0.260575	0.19892	-1.31	0.19021	
sex	0.185654	0.069827	2.659	0.00784	**
age	-0.010261	0.002443	-4.201	2.66E-05	***
Ebola Ab+	0.489036	0.093638	5.223	1.76E-07	***

	Chisq	Pr(>Chisq)	
mod			
mod + EbAb	27.146	1.89E-07	***

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Association Screening Analysis
(Vaumourin *et al.*, 2014)

- 3 advantages:
  1. Power!!!
  2. More than just pairwise associations

Gabon Results

Interesting patterns identified:

2. *Loa loa* and *Mansonella perstans* are tightly associated, but the rarity of solo *M. perstans* infections and abundance data suggests *L.loa* plays a within-host facultative role. Furthermore, when *Mp* and *Ll* co-infect, they appear more often in hosts with lower evidence of exposure to other parasites. * yet to be verified, tests still underway

SCN + Rarefaction

														% data sampled										
														10%					→				100%	RR
Association:	ll	fp	ma	hc	ht	eb	rf	de	wn	ch														
Order	ll	fp	ma	hc	ht	eb	rf	de	wn	ch	As	Direction		VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VSA
1018								1	1	0	#	Frequent		0	0	0	0	0	1	1	1	1	1	5
880			1	0	0	1	0	0	0	0	#	Frequent		0	0	0	0	0	0	1	1	1	1	4
1017								1	1	1	#	Frequent		0	0	0	0	0	0	1	1	1	1	4
1014							1	0	1	0	#	Frequent		0	0	0	0	0	0	0	1	1	1	3
112	1	1	1	0	0	1	0	0	0	0	#	Frequent		0	0	0	0	0	0	0	1	1	1	3
892			1	0	0	0	0	1	0	0	#	Rare		0	0	0	0	0	0	0	0	1	1	2
1020								1	0	0	#	Rare		0	0	0	0	0	0	0	0	1	1	2
256	1	1	0	0	0	0	0	0	0	0	#	Frequent		0	0	0	0	0	0	0	0	1	1	2
830			1	1	0	0	0	0	1	0	#	Rare		0	0	0	0	0	0	0	0	1	1	2
505	1	0	0	0	0	0	0	1	1	1	#	Random		0	0	0	0	0	0	0	0	0	1	1
506	1	0	0	0	0	0	0	1	1	0	#	Frequent		0	0	0	0	0	0	0	0	0	1	1
126	1	1	1	0	0	0	0	0	1	0	#	Frequent		0	0	0	0	0	0	0	0	0	1	1
182	1	1	0	1	0	0	1	0	1	0	#	Random		0	0	0	0	0	0	0	0	0	1	1
298	1	0	1	1	0	1	0	1	1	0	#	Random		0	0	0	0	0	0	0	0	0	1	1
312	1	0	1	1	0	0	1	0	0	0	#	Random		0	0	0	0	0	0	0	0	0	1	1
1016							1	0	0	0	#	Rare		0	0	0	0	0	0	0	0	0	1	1
352	1	0	1	0	1	0	0	0	0	0	#	Frequent		0	0	0	0	0	0	0	0	0	1	1
415	1	0	0	1	1	0	0	0	0	1	#	Random		0	0	0	0	0	0	0	0	0	1	1
757		1	0	0	0	0	1	0	1	1	#	Random		0	0	0	0	0	0	0	0	0	1	1
489	1	0	0	0	0	1	0	1	1	1	#	Random		0	0	0	0	0	0	0	0	0	0	0
695		1	0	1	0	0	1	0	0	1	#	Random		0	0	0	0	0	0	0	0	0	0	0
469	1	0	0	0	1	0	1	0	1	1	#	Random		0	0	0	0	0	0	0	0	0	0	0
480	1	0	0	0	1	0	0	0	0	0	#	Frequent		0	0	0	0	0	0	0	0	0	0	0
633		1	1	0	0	0	0	1	1	1	#	Random		0	0	0	0	0	0	0	0	0	0	0
496	1	0	0	0	0	1	0	0	0	0	#	Rare		0	0	0	0	0	0	0	0	0	0	0
512	1	0	0	0	0	0	0	0	0	0	#	Rare		0	0	0	0	0	0	0	0	0	0	0

Gabon Results

Interesting patterns identified:

2. *Loa loa* and *Mansonella perstans* are tightly associated, but the rarity of solo *M. perstans* infections and abundance data suggests *L.loa* plays a within-host facultative role. Furthermore, when *Mp* and *LI* co-infect, they appear more often in hosts with lower evidence of exposure to other parasites. * yet to be verified, tests still underway

Generalized Linear Models:

Response: **Number of other Abs present (HTLV,WNV,DENV,CHKV,RFV)**

Co-Infection

Fixed effects:	Estimate	df	Deviance	Resid.Df	Deviance	Pr(>Chi)	
Null (poisson)	-1.142	1596	1615.9			1.55E-14	***
age	0.019	1	84.315	1595	1531.6	< 2.20E-16	***
sex (male)	0.038	1	0.049	1594	1531.6	0.825604	
department		14	68.795	1580	1462.8	3.19E-09	***
malaria+	-178	1	8.687	1579	1454.1	0.003206	**
Eb Ab+	0.011	1	0.004	1578	1454.1	0.951932	
Fil_coinfection	-0.525	1	7.516	1577	1446.6	0.006115	**

M. perstans

Fixed effects:	Estimate	df	Deviance	Resid.Df	Deviance	Pr(>Chi)	
Null (poisson)	-1.124	1596	1615.9			4.21E-14	***
age	0.018	1	84.315	1595	1531.6	< 2.20E-16	***
sex (male)	0.03	1	0.049	1594	1531.6	0.825604	
department		14	68.795	1580	1462.8	3.19E-09	***
malaria+	-0.186	1	8.687	1579	1454.1	0.003206	**
Eb Ab+	0.008	1	0.004	1578	1454.1	0.951932	
M_perstans Inf.	-0.112	1	1.038	1577	1453	0.308375	

Loa loa

Fixed effects:	Estimate	df	Deviance	Resid.Df	Deviance	Pr(>Chi)	
Null (poisson)	-1.139	1596	1615.9			1.47E-14	***
age	0.018	1	84.315	1595	1531.6	< 2.20E-16	***
sex (male)	0.011	1	0.049	1594	1531.6	0.825604	
department		14	68.795	1580	1462.8	3.19E-09	***
malaria+	-0.191	1	8.687	1579	1454.1	0.003206	**
Eb Ab+	0.008	1	0.004	1578	1454.1	0.951932	
Loa_loa Inf.	0.07	1	1.016	1577	1453.1	0.313391	

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- 3 advantages:
  1. Power!!!
  2. More than just pairwise associations
  3. Potential for detection of directionality

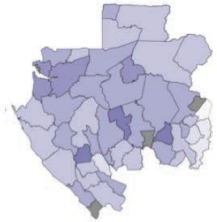
Gabon Results

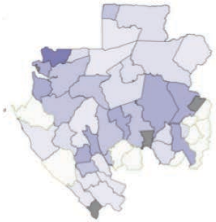
Interesting patterns identified:

2. *Loa loa* and *Mansonella perstans* are tightly associated, but the rarity of solo *M. perstans* infections and abundance data suggests *L.loa* plays a within-host facultative role.

- Eukaryotes (active infection)

Loa loa (22%) *Mansonella perstans* (10%)





SCN + Rarefaction

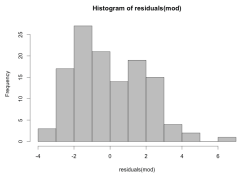
Association Order	ll	fp	Direction	% data sampled 10% → 100%	robustness score (RR)
1	1	1	Frequent		5
2	1	0	Rare		0
3	0	1	Rare		1
4	0	0	Frequent		0

Analysis of Variance Table (terms added sequentially)

Response: log nb_ManPers

Variables	Df	Sum Sq	MeanSq	F value	Pr(>F)	
sex	1	1.67	1.667	0.406	0.525	
age	1	0.43	0.428	0.104	0.7473	
log nb_Loaloa	1	35.04	35.04	8.541	0.0042	**
Residuals	119	488.2	4.103			

model residuals



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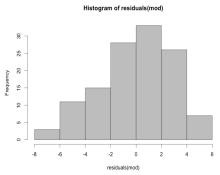

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The reliability of observational approaches for detecting interspecific parasite interactions: comparison with experimental results

Andy Fenton [a,*], Sarah C.L. Knowles [b], Owen L. Petchey [c], Amy B. Pedersen [d]

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[b] Department of Infectious Disease Epidemiology, Imperial College London, St. Mary's Campus, Norfolk Place, London W2 1PG, UK
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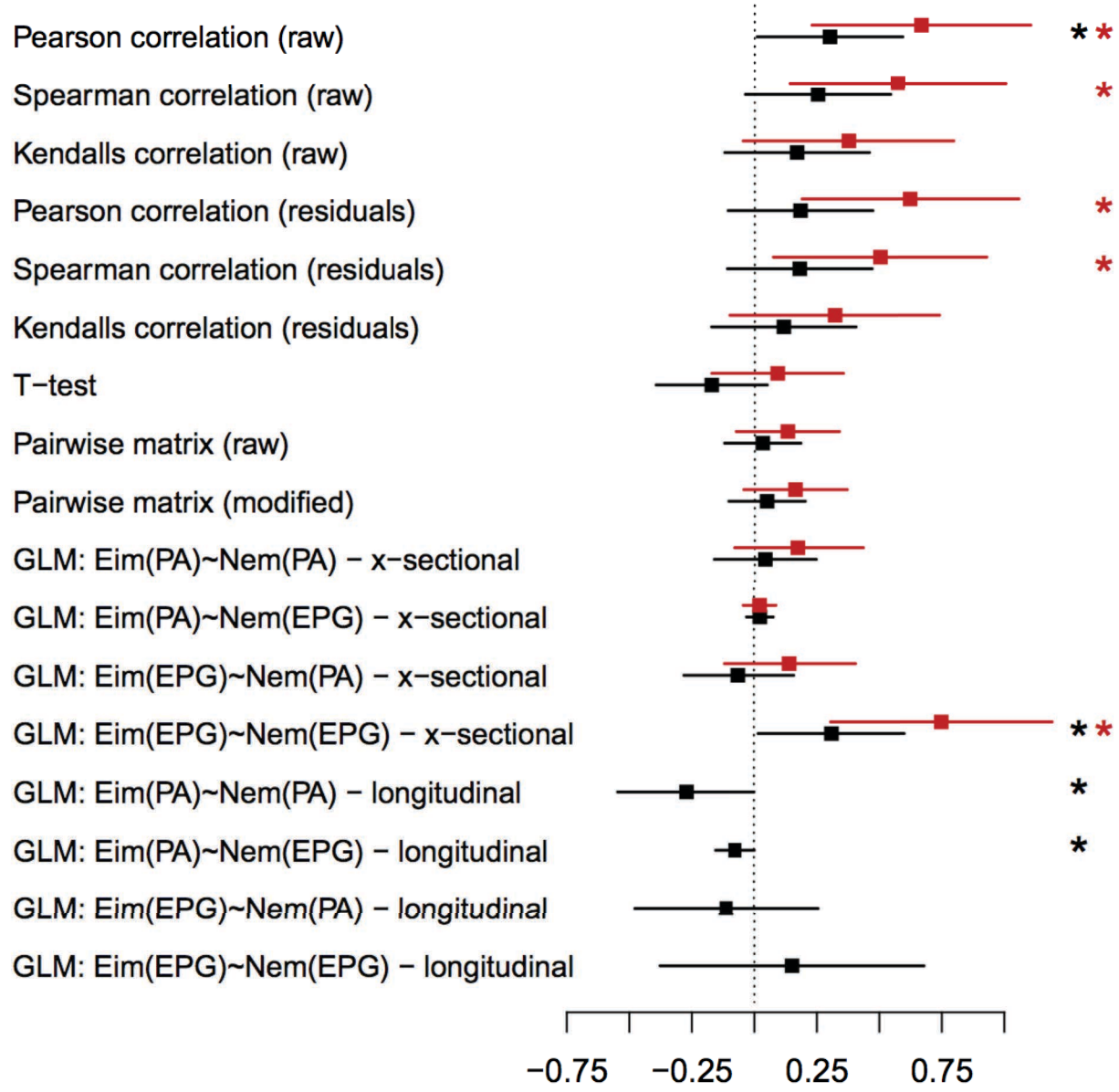
ABSTRACT

Interactions among coinfecting parasites have the potential to alter host susceptibility to infection, the progression of disease and the efficacy of disease control measures. It is therefore essential to be able to accurately infer the occurrence and direction of such interactions from parasitological data. Due to logistical constraints, perturbation experiments are rarely undertaken to directly detect interactions, therefore a variety of approaches are commonly used to infer them from patterns of parasite association


Pearson correlation (raw)
Spearman correlation (raw)
Kendalls correlation (raw)
Pearson correlation (residuals)
Spearman correlation (residuals)
Kendalls correlation (residuals)
T−test
Pairwise matrix (raw)
Pairwise matrix (modified)
GLM: Eim(PA)~Nem(PA) − x−sectional
GLM: Eim(PA)~Nem(EPG) − x−sectional
GLM: Eim(EPG)~Nem(PA) − x−sectional
GLM: Eim(EPG)~Nem(EPG) − x−sectional
GLM: Eim(PA)~Nem(PA) − longitudinal
GLM: Eim(PA)~Nem(EPG) − longitudinal
GLM: Eim(EPG)~Nem(PA) − longitudinal
GLM: Eim(EPG)~Nem(EPG) − longitudinal
* *
*
*
*
* *
*
*
−0.75
−0.25
0.25
0.75
Nematode−*Eimeria* interaction effect size (Hedge's *g*)

Gabon Results

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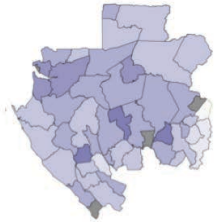

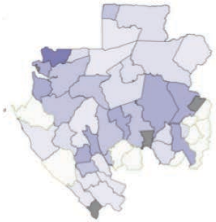

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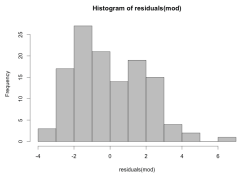

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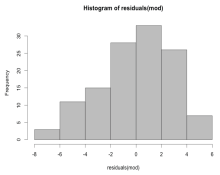
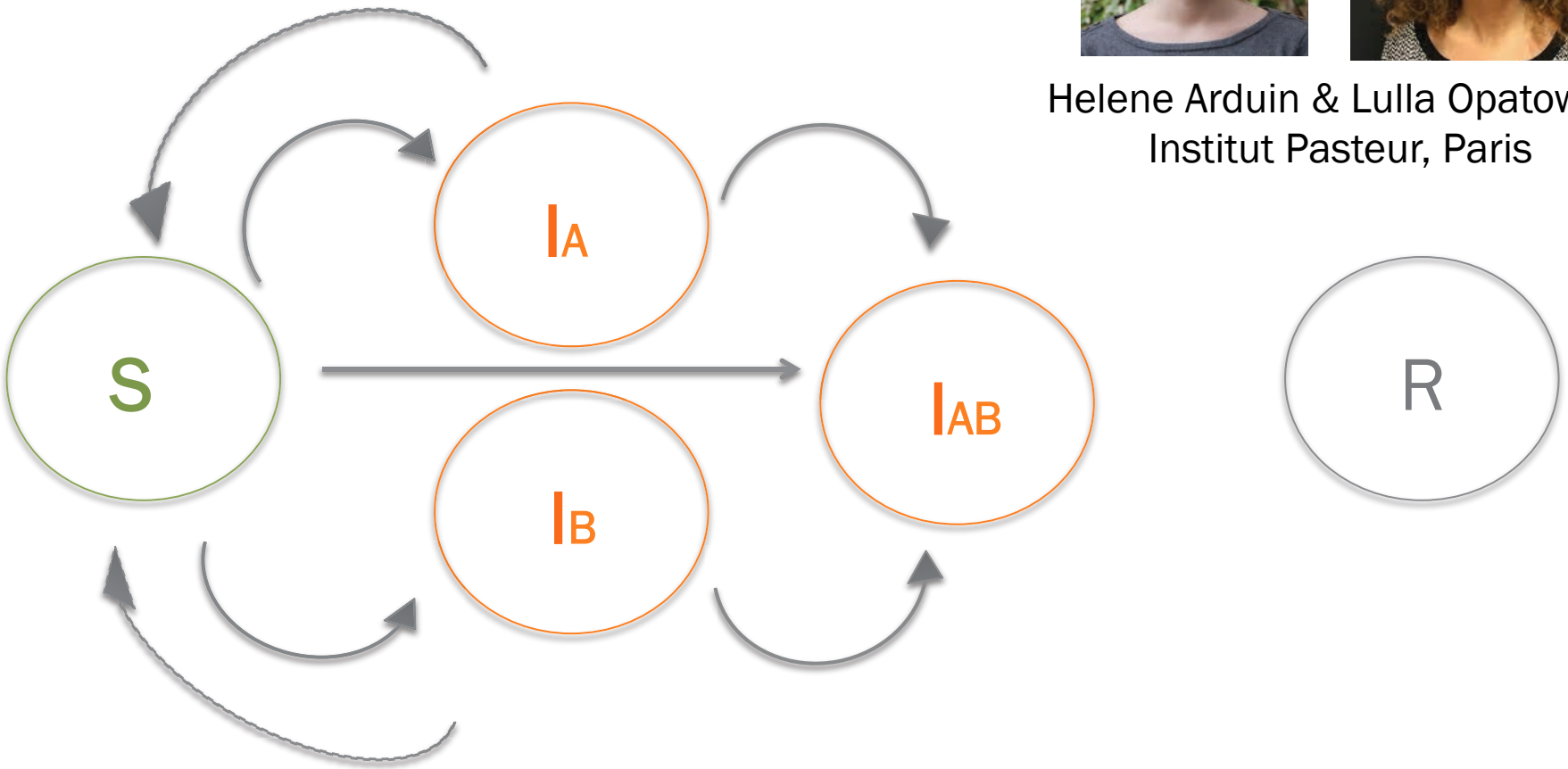
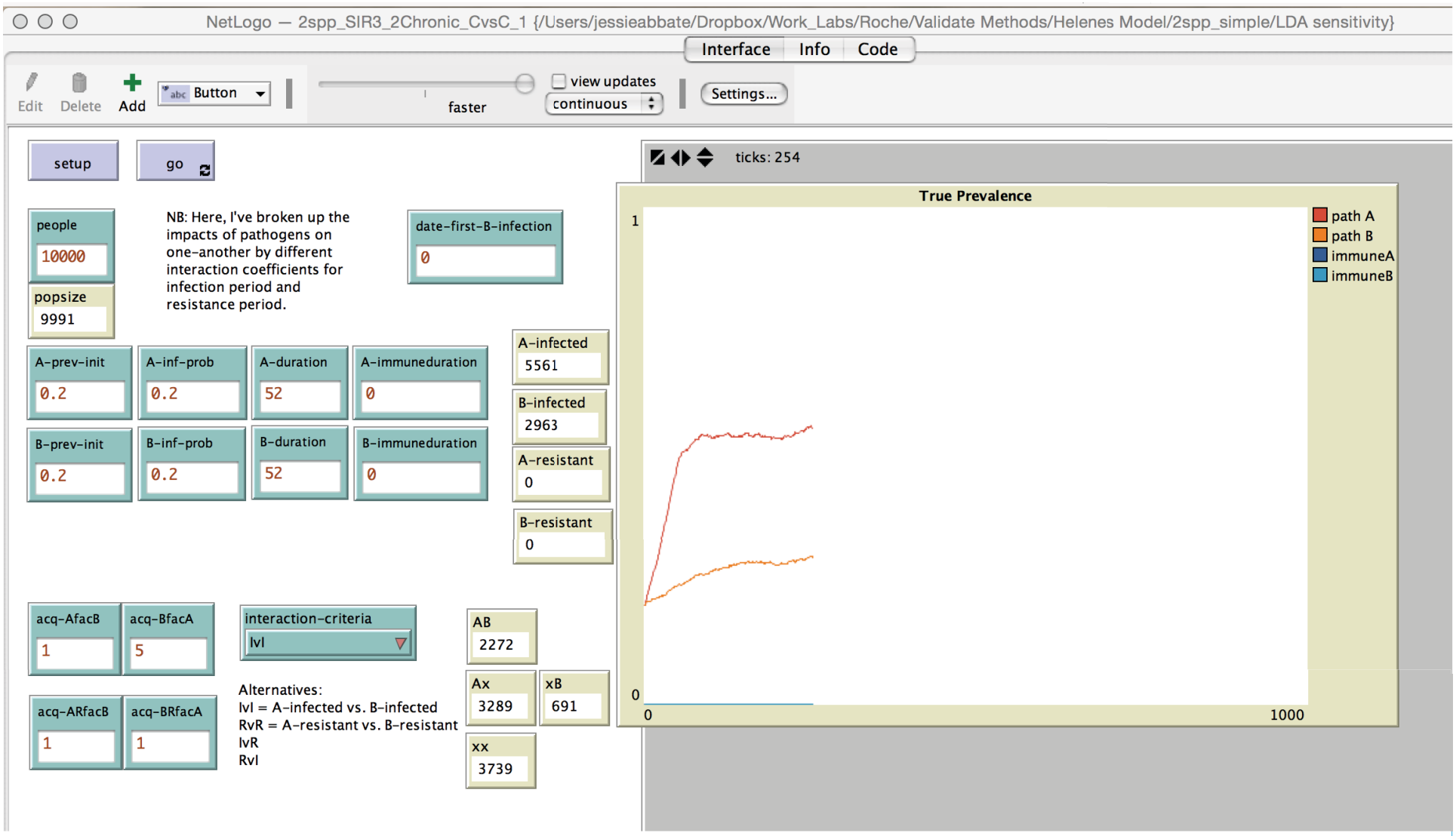


Individual-based Model

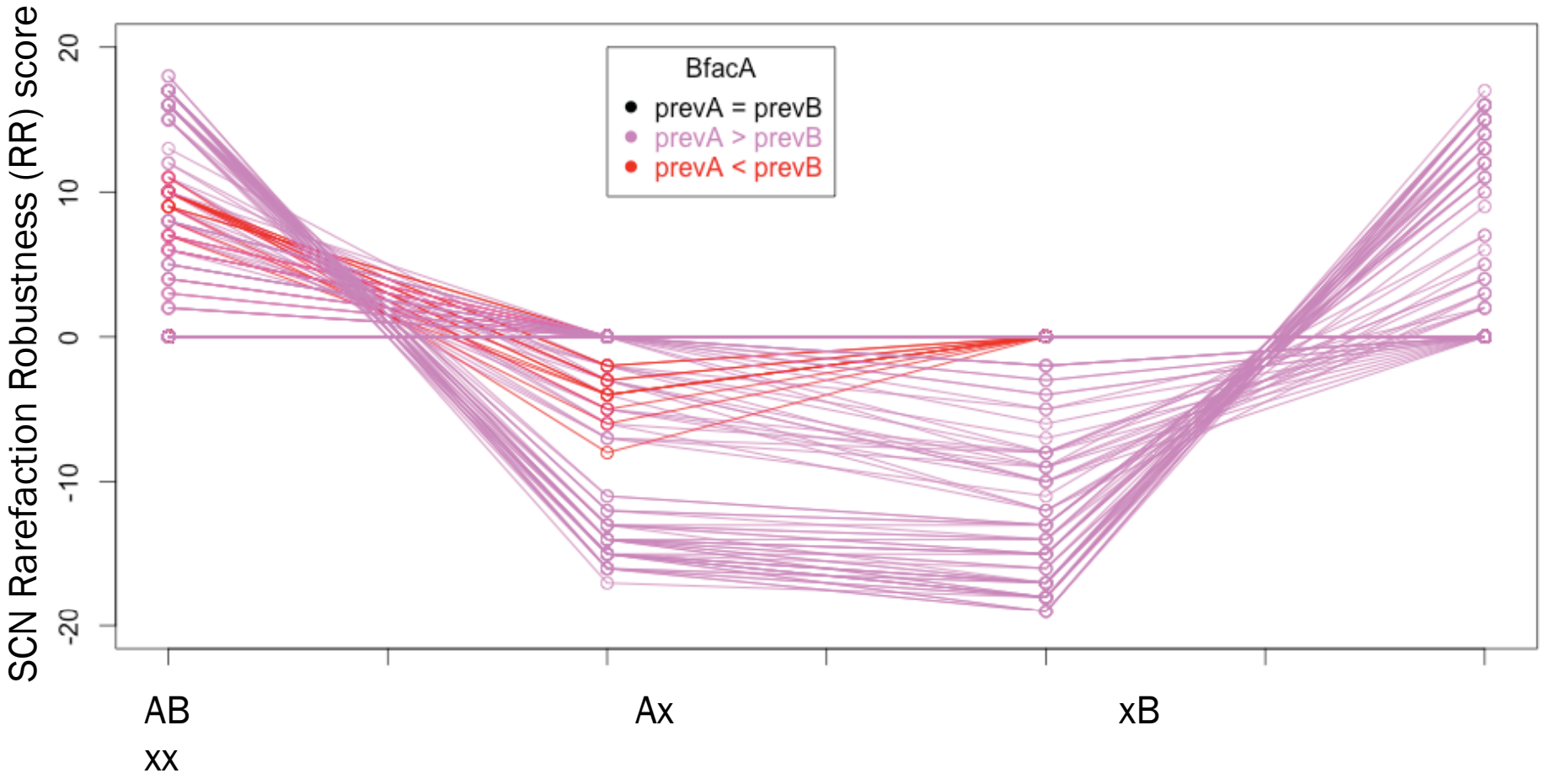
Helene Arduin & Lulla Opatowski
Institut Pasteur, Paris



Individual-based Model

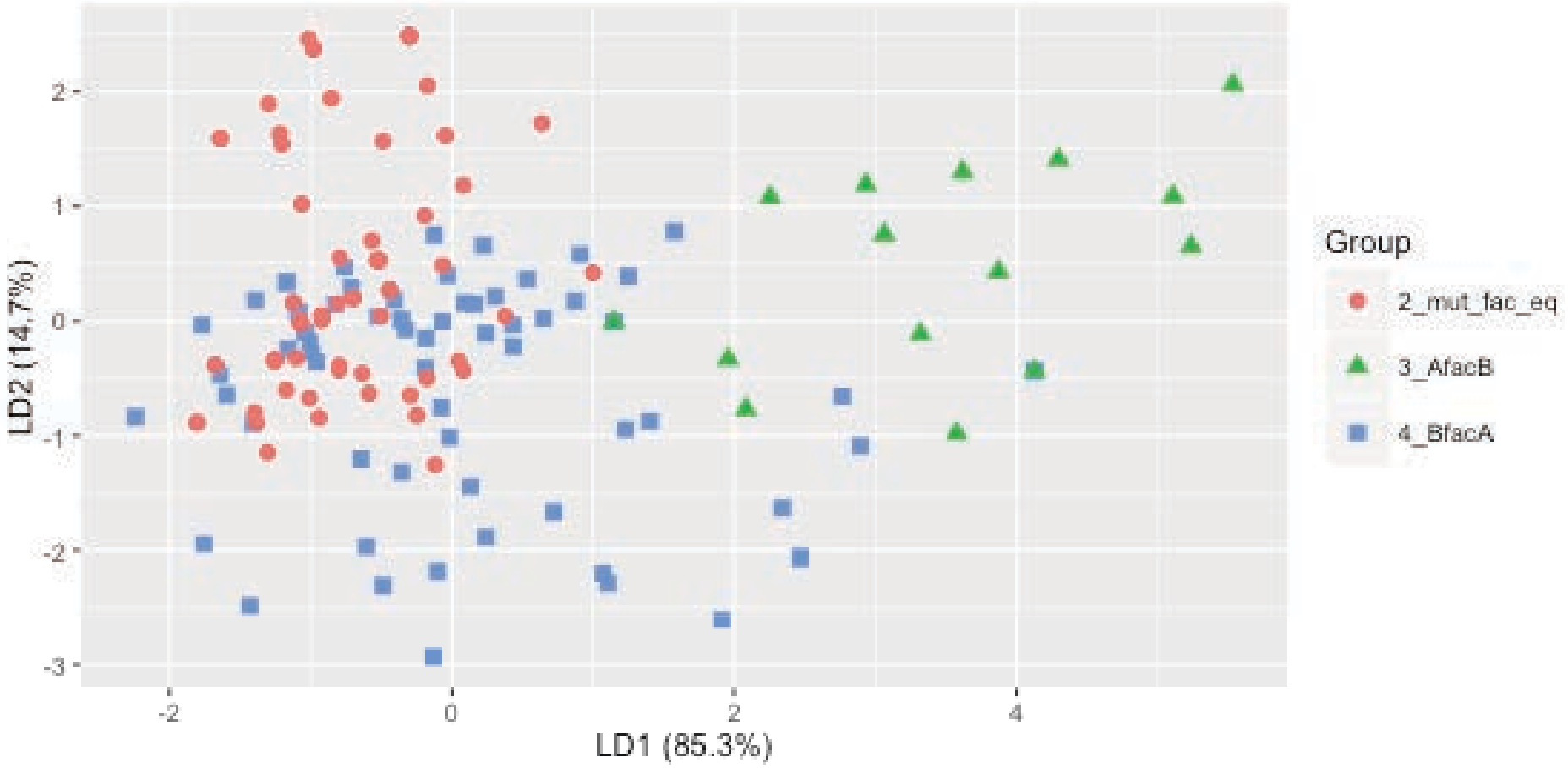


Simulation Results



Simulation Results

LINEAR DISCRIMINANT ANALYSIS



LL facilitates FP ~0.87

How can we detect pathogen-pathogen interactions in humans (and other species) using minimally-invasive techniques?

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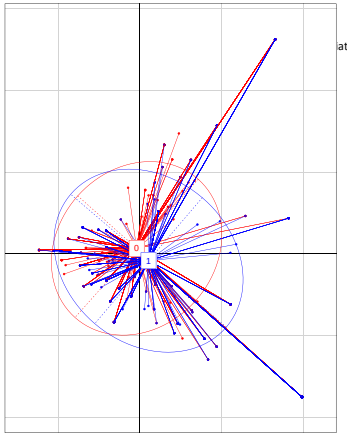
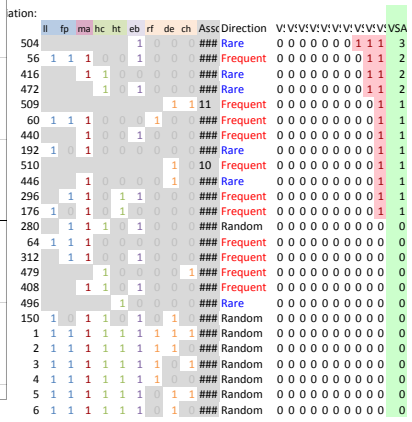
"pipeline" statistique

MCA + SCN Rarefaction + Regression SEM





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56	1	1	1	0	0	1	0	0	0	###	Frequent	0	0	0	0	0	0	0	0	1	1	2
416			1	1	0	0	0	0	0	###	Rare	0	0	0	0	0	0	0	0	1	1	2
472				1	0	1	0	0	0	###	Rare	0	0	0	0	0	0	0	0	1	1	2
509							1	1	11		Frequent	0	0	0	0	0	0	0	0	0	1	1
60	1	1	1	0	0	0	1	0	0	###	Frequent	0	0	0	0	0	0	0	0	0	1	1
440			1	0	0	1	0	0	0	###	Frequent	0	0	0	0	0	0	0	0	0	1	1
192	1	0	1	0	0	0	0	0	0	###	Rare	0	0	0	0	0	0	0	0	0	1	1
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446			1	0	0	0	0	1	0	###	Rare	0	0	0	0	0	0	0	0	0	1	1
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496					1	0	0	0	0	###	Rare	0	0	0	0	0	0	0	0	0	0	0
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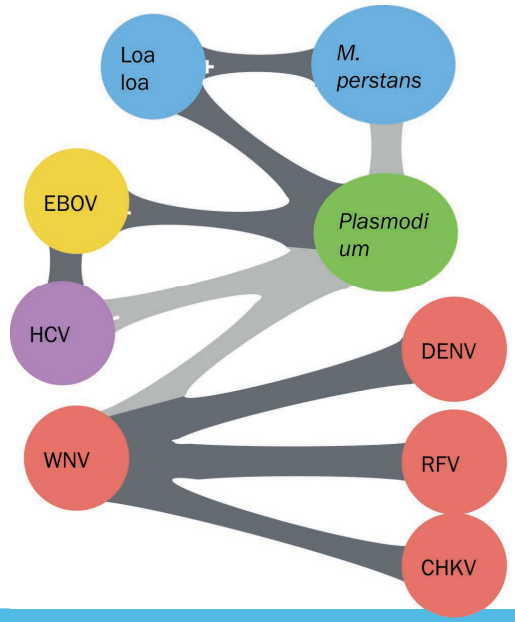

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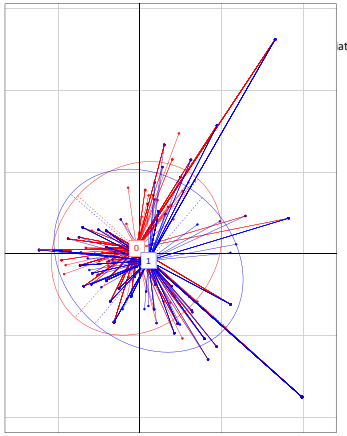

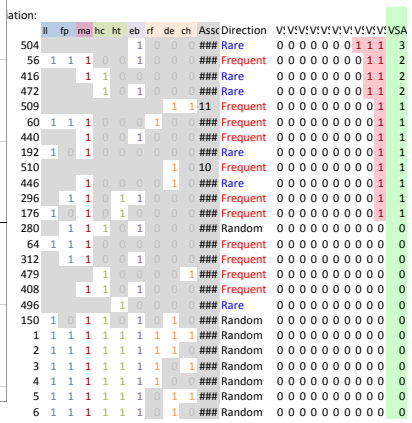

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504						1	0	0	0	###	Rare	0	0	0	0	0	0	1	1	1	3
56	1	1	1	0	0	1	0	0	0	###	Frequent	0	0	0	0	0	0	0	1	1	2
416			1	1	0	0	0	0	0	###	Rare	0	0	0	0	0	0	0	1	1	2
472				1	0	1	0	0	0	###	Rare	0	0	0	0	0	0	0	1	1	2
509							1	1	11		Frequent	0	0	0	0	0	0	0	0	1	1
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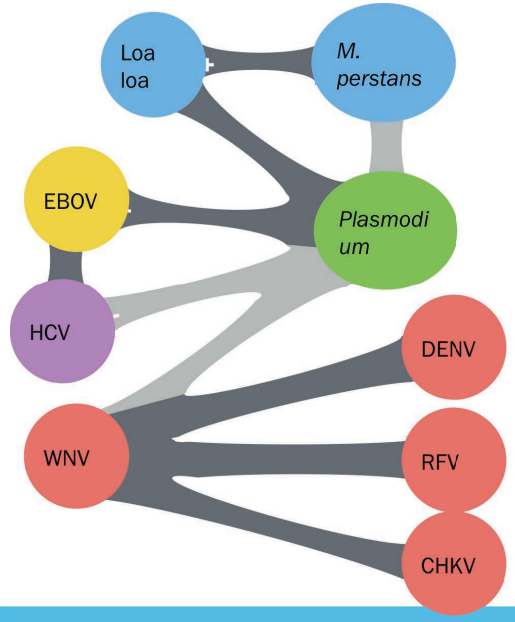

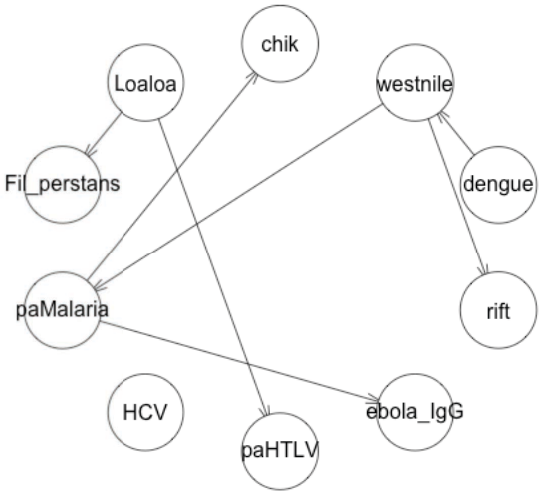

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“pipeline” statistique → Modélisation d’hypothèses

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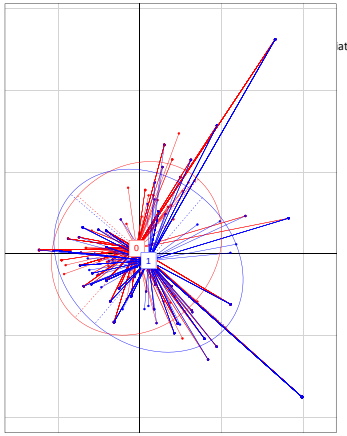
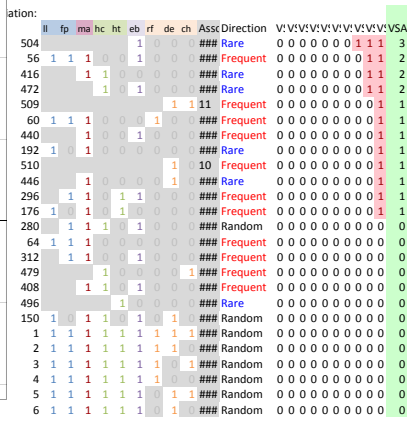
Modèle IBM





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296		1	1	0	1	1	0	0	0	###	Frequent	0	0	0	0	0	0	0	0	1		1
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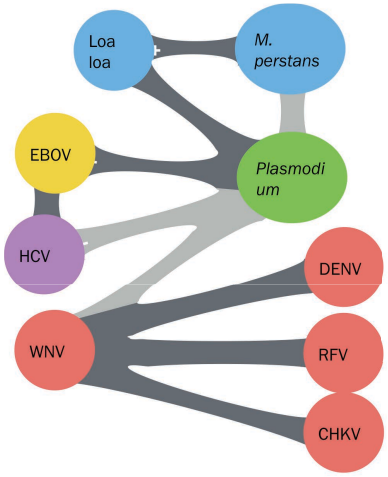
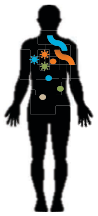
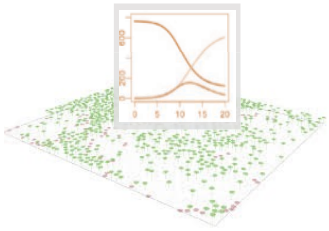


Interactions intra-hôtes + Interactions inter-hôtes





Distribution