

# The ecology of emerging diseases: a data mining approach

**Modeling the Complexity of Disease** 

Chris Stephens

C3 – Centro de Ciencias de la Complejidad y Instituto de Ciencias Nucleares, UNAM Talk LSHTM 23/07/2013



# Who are we?

#### Complex systems and data mining group

- 1.- Dr. Christopher R. Stephens
- 2.- M. en. C. Hugo Flores
- 3.- M. en C. Raúl Sierra Alcocer
- 4.- M. en C. Constantino González Salazar
- 5.- Dra. Ana Sanchez
- 6.- Dr. David Rosenblueth
- 7.- Dr. Manuel Beltran (U. of Arizona)

#### <u>Grupo del Laboratorio de sistemas de información geográfica del</u> <u>Instituto de Biología de la UNAM.</u>

- 8.- Dr. Víctor Sánchez-Cordero
  9.- Dr. Ángel Rodríguez Moreno
  10.- Dr. José Juan Flores Martínez
  11.- Dr. Gabriel Granados Gutiérrez
  12.- Dra. Camila González Rosas (Universidad de los Andes, Columbia)
  13.- Dr. Carlos Napoleón Ibarra Cerdeña (INSP, Tapachula)
- 14.- Est. Biól. Ruth Areli Gómez Rodríguez
- 15.- Est. Biól. María Azucena Trinidad Flores

### **Complexity and Public** Health Program – C3, UNAM



# Who are we?

<u>Grupo del laboratorio de inmunoparasitología del Departamento de Medicina Experimental de la Facultad de Medicina</u> <u>en la UNAM.</u>

- 16.- Dra. Ingeborg Becker
- 17.- Dra. Miriam Berzunza Cruz
- 18.- QFB. Dulce Jocelyn Bailón Martínez
- 19.- M. en C. Cristina Cañedo Guzmán

#### El Centro Regional de Investigación del Instituto Nacional de Salud Pública (Tapachula, Chis.)

- 20.- Dra. Janine M. Ramsey Willoquet
- 21.- Dr. Carlos Félix Marina Fernández
- 22.- Dra. Teresa Ordoñez
- 23.- Keynes De la Cruz Félix



# Who are we?

#### <u>Grupo de Tabasco: División Académica de Ciencias Biológicas. Universidad</u> <u>Juárez Autónoma de Tabasco</u>

24.- Dr. Mircea Gabriel Hidalgo Mihart 25.- Dra. Cristina Domingo Balcells

#### Grupo de Monterrey: Laboratorio de Entomología médica, Depto. de Zoología de Invertebrados. Facultad de Ciencias Biológicas, Universidad Autónoma de Nuevo León

26.- Dr. Eduardo A. Rebollar Téllez 27.- Estudiante Jorge Jesús Rodriguez Rosas

#### <u>Grupo de Jalisco: Centro Universitario de la Costa Sur. Universidad de</u> <u>Guadalajara.</u>

28.- Dr. Luis Ignacio Iñiguez Dávalos 29.- Biól. Pilar Ibarra 30.- Biól. María Magdalena Ramírez Martínez

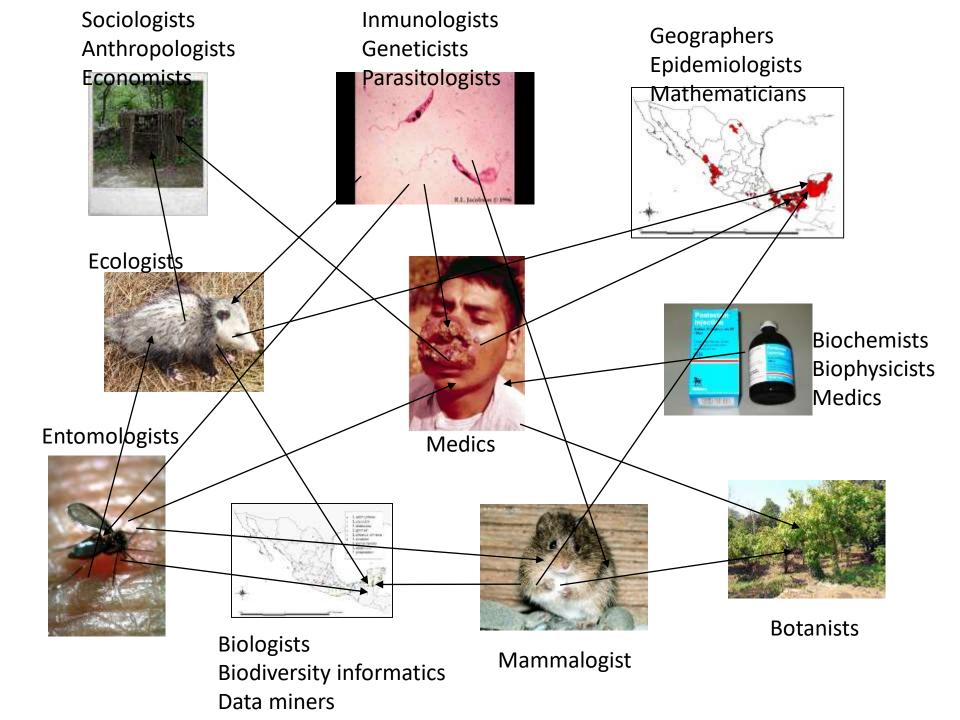
#### London School of Hygiene and Tropical Medicine

31.- Dr. Michael Gaunt



# The Complexity of Disease and the Need for Transdisciplinarity

From the micro to the macro and back again





### What are our goals? The Santa Clause list

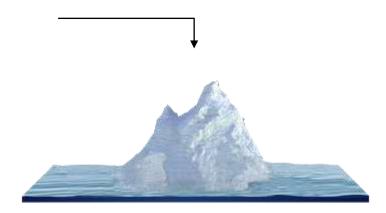
Where will diseases emerge or re-emerge – why, when, what can we do about it and how do we know it's working?

- · We want to predict, for instance
  - Disease reservoirs and vectors, their interactions and their relative importance
  - Spatio-temporal behaviour of disease and associated risk factors
  - Dispersal characteristics
  - Socio-demographic/economic risk factors
  - Genetic susceptibility (at all levels)

 We want an integrated systems analysis that takes into account the complex nature of disease and we want to understand



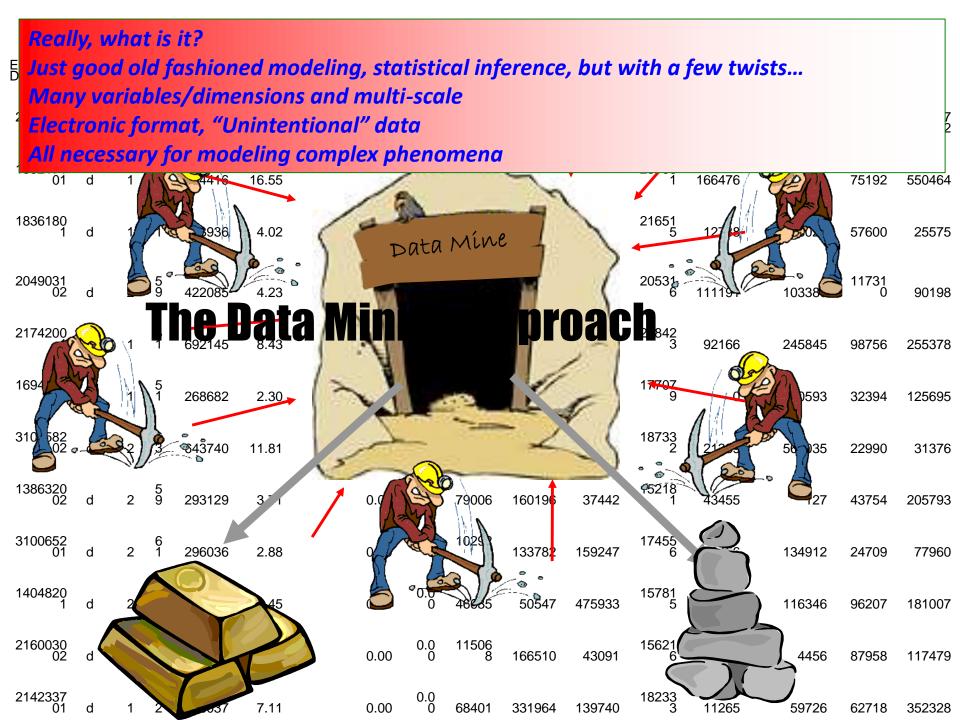
Known reservoirs Known vectors Known cases Known risk factors





Known reservoirs Known vectors Known cases Known risk factors Unknown reservoirs Unknown vectors Unknown cases Unknown risk factors







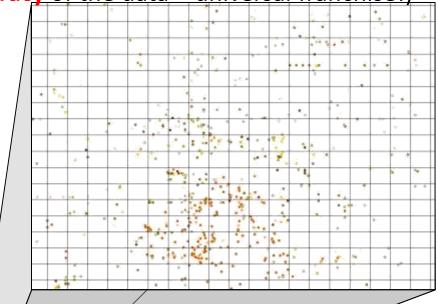
# But what are we going to mine...!



# Anything and everything!

- Collection data
- \* Ecological niche data
- Ecological niche model data
- Socio-economic data
- Socio-demographic data
- \* Phenotypic data
- Vegetable and crop cover
- A Geographical data
- Medical and public health data...

(A democracy of the data – universal franchise!)



The data are represented in space and time – spatial data mining



But all data are not created equal...

# Different sources

- Different location, data base, access,...
- Different data type categorical, metric
- Different spatial resolution
  - Explicit e.g., pixel by pixel in environmental layers
  - Implicit 30,000,000 data points versus 30
    - Quality versus quantity
    - Abiotic versus biotic

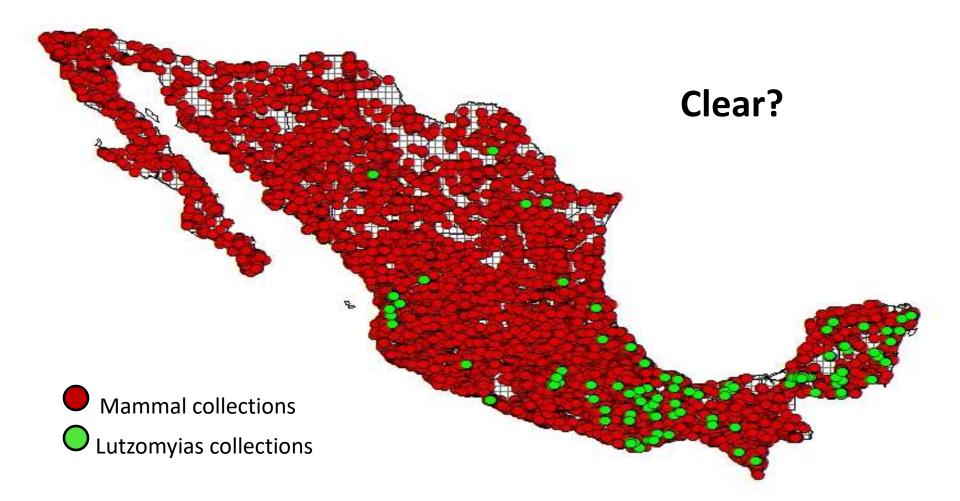
Need to avoid the tyranny of the majority and protect minority rights! Also, we need to be able to compare apples with apples!



- But the real Niche Space of a disease is VERY big!
- Where do we start?
- With the biotic...
- With the "ecological" part, reservoirs and vectors and all that...



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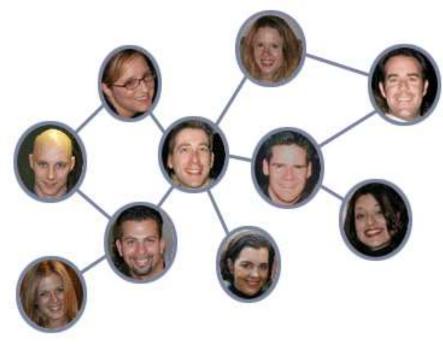




# You can judge a man

# by his "friends"

or his "enemies", or "parasites", or "prey" or "predators" or...





### **Typical Ecological Network**

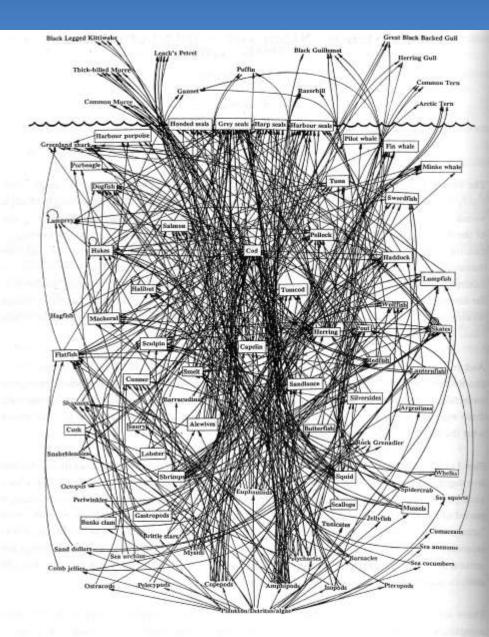
Food web associated with Cod for northwest Atlantic

Author(s): Prof. David Lavigne

Institution: Natural Sciences and Engineering Research Council

Visualization of *known* interactions at the species level

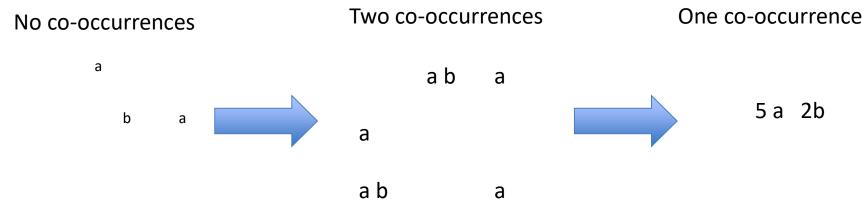
No spatio-temporal input



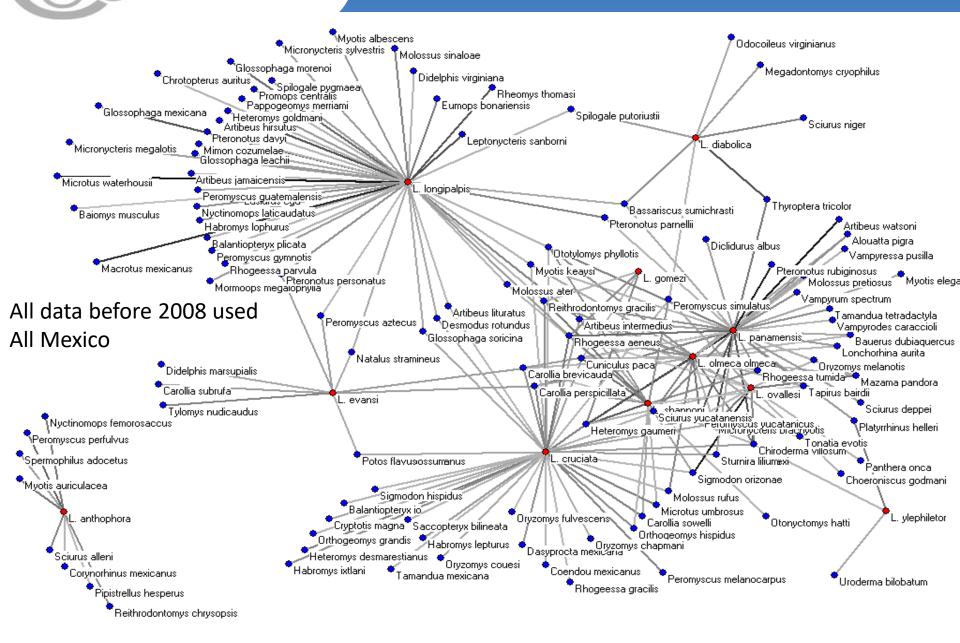


### Using Networks to Infer Reservoir-Vector Interactions

- Take nodes to be...
  - Species, other taxonomic or phylogenetic groupings, groupings by phenotypic characteristics,
- Take links to be a statistical measure of spatial (temporal) co-occurrence
  - P(Y|X), epsilon(Y|X), P(A,B|C,D), epsilon(Z|X,Y)
  - What is a high/low degree of co-occurrence?
  - What spatial (temporal) resolution? (When do things co-occur?)



### Who's friends with Lutzomyias?



### **Predicting Reservoirs**

The 150 (out of 427) "best friends" of Lutzomyia as a genera. The model works on known results.

	Mammals	Epsilon	Conf.		
1	Eira barbara	10.1683			
	Rhogeessa aeneus	9.3649			
	Artibeus intermedius	9.1628			
	Reithrodontomys gracilis	8.8921	Yes		
	Carollia sowelli	8.8303	103		
	Heteromys gaumeri	8.8000	Yes		
	Peromyscus mexicanus	8.7859	100		
	Heteromys desmarestianu	8.7164	Yes		
	Molossus rufus	8.6277	100		
	Glossophaga soricina	8.5713			
	Carollia perspicillata	8.5030			
12	Orthogeomys hispidus	8.3468			
	Pteronotus parnellii	8.1632			
	Desmodus rotundus	8.1519			
	Dasyprocta mexicana	8.1128			
	Sturnira lilium	8.0290			
	Dermanura phaeotis	8.0055			
	Dasyprocta punctata	7.9678			
	Oryzomys couesi	ata 7.9678 7.7253			
	Potos flavus	7.7246			
	Conepatus semistriatus	7.6879			
	Ototylomys phyllotis	7.5587	Yes		
	Ateles geoffroyi	7.4787	100		
24	Cryptotis magna	7.4207			
25	Cuniculus paca	7.3220			
26	Lampronycteris brachyotis	7.2852			
	Sigmodon hispidus	7.2805	Yes		
	Peromyscus yucatanicus	7.2486	Yes		
	Oryzomys chapmani	7.1242			
	Didelphis virginiana	7.1150			
	Peromyscus melanocarpu	7.0260			
	Microtus umbrosus	6.9630			
33	Thyroptera tricolor	6.9630			
34	Nasua narica	6.8953			
35	Megadontomys cryophilus	6.6830			
36	Oryzomys alfaroi	6.6816			
37	Sorex veraepacis	6.6797			
38	Carollia subrufa	6.6316			
39	Peromyscus aztecus	6.6173			
40	Didelphis marsupialis	6.4390	Yes		
41	Sciurus yucatanensis	6.3865			
42	Philander opossum	6.2546			
43	Habromys ixtlani	6.1120			
	Microtus waterhousii	6.1120			
45	Pteronotus rubiginosus	6.1120			
46	Reithrodontomys microdor				
47	Coendou mexicanus	6.0268			
	Centurio senex	6.0076			
	Artibeus jamaicensis	5.9786			
50	Glossophaga morenoi	5.8847			

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	Mammals	Epsilon	Conf
51	Molossus sinaloae	5.8518	
	Artibeus lituratus	5.8422	
53	Mormoops megalophylla	5.8374	
54	Habromys lepturus	5.7848	
55	Myotis keaysi	5.6148	
	Chiroderma villosum	5.5562	
57	Tamandua mexicana	5.4845	
58	Tylomys nudicaudus	5.4510	
59	Saccopteryx bilineata	5.2984	
	Macrotus mexicanus	5.2472	
61	Sciurus aureogaster	5.2267	
	Baiomys musculus	5.2092	
	Rhogeessa tumida	5.1950	
	Sciurus deppei	5.1414	
65	Dermanura watsoni	5.1338	
	Otonyctomys hatti	5.1338	
67	Orthogeomys grandis	5.0556	
	Alouatta palliata	5.0457	
69	Choeroniscus godmani	5.0457	
	Peropteryx macrotis	5.0457	
	Pteronotus personatus	5.0266	
	Lontra longicaudis	4.9330	
	Reithrodontomys mexicanu	4.9120	
	Oryzomys rostratus	4.8681	
	Mimon cozumelae	4.8327	
	Pteronotus davyi	4.7943	
	Herpailurus yagouaroundi	4.7100	
	Glossophaga leachii	4.6849	
	Rhogeessa gracilis	4.6317	
	Sylvilagus brasiliensis	4.6317	
	Hodomys alleni	4.5155	
	Leopardus wiedii	4.4420	
	Peromyscus simulatus	4.4195	
	Sigmodon alleni	4.3707	
	Bassariscus sumichrasti	4.3110	
	Oryzomys fulvescens	4.3110	
	Diphylla ecaudata	4.3013	
	Oryzomys melanotis	4.2907	Yes
	Micronycteris microtis	4.2338	
	Mazama americana	4.2274	
	Microtus oaxacensis	4.2061	
_	Rheomys thomasi	4.2061	
	Oryzomys saturatior	4.2061	
	Myotis elegans	4.2024	
	Oligoryzomys fulvescens	4.1984	
	Natalus stramineus	4.0626	
	Balantiopteryx io	4.0522	
	Nyctinomops laticaudatus	4.0522	
	Tlacuatzin canescens	4.0119	
100	Odocoileus virginianus	3.9265	

	Mammals	Epsilon	Conf
101	Balantiopteryx plicata	3.8590	
102	Peromyscus leucopus	3.7994	
103	Sturnina ludovici	3.7888	
104	Enchisthenes hartii	3.6929	
105	Vampyrodes caraccioli	3.6929	
	Eptesicus furinalis	3.6453	
	Liomys pictus	3.6107	
	Glossophaga commissaris	3.4861	
	Lonchorhina aurita	3.4781	
	Phyllostomus discolor	3.4781	
	Peromyscus gymnotis	3.4516	
	Anoura geoffroyi	3.4201	
	Platyrrhinus helleri	3.3586	
	Eumops bonariensis	3.3398	
	Sciurus variegatoides	3.3398	
	Uroderma bilobatum	3.3373	
	Lasiurus intermedius	3.2197	
	Lasiurus ega	3.1739	
	Peromyscus megalops	3.1410	
	Eumops glaucinus	3.0564	<u> </u>
	Urocyon cinereoargenteus		
	Procyon lotor	2.9697	
	Hylonycteris underwoodi		
		2.9343	
	Rhynchonycteris naso	2.8580	
	Eptesicus brasiliensis	2.8106	
	Myotis albescens	2.8106	
	Lophostoma evotis	2.8106	
	Tapirus bairdii	2.8106	
	Vampyrum spectrum	2.8106	
	Marmosa mexicana	2.7731	Yes
	Peromyscus furvus	2.7731	
	Myotis velifera	2.5757	
	Spilogale putorius	2.5411	
	Microtus mexicanus	2.5268	
	Dasypus novemcinctus	2.4725	
	Myotis nigricans	2.4704	
	Lophostoma brasiliense	2.4407	
	Diclidurus albus	2.4407	
	Sciurus niger	2.4407	
	Leptonycteris curasoae	2.4268	
	Nyctomys sumichrasti	2.4026	
142	Sigmodon mascotensis	2.3815	
	Alouatta pigra	2.3374	
144	Peromyscus melanophrys	2.2204	
	Dermanura tolteca	2.1920	
	Trachops cirrhosus	2.1663	
	Bauerus dubiaquercus	2.1612	
	Spilogale pygmaea	2.1612	
	Leptonycteris nivalis	2.1402	
	Sylvilagus floridanus	2.1002	



## But how to test it...? **The Emerging Disease production** line

Links to IMSS and INSP

Close relationship with

Requires large, well-organized interdisciplinary team

Data Mining: public health authorities Predictive models, and private sector **Risk factors** Field work : samples Five groups distributed throughout Mexico DF, Chiap., NL, Jal., Tab. Laboratory analysis Solutions: Decision support systems Over 1200 mammals Two laboratories **A** Treatments collected from over PCR tests on samples Intelligent software 70 species

for different diseases

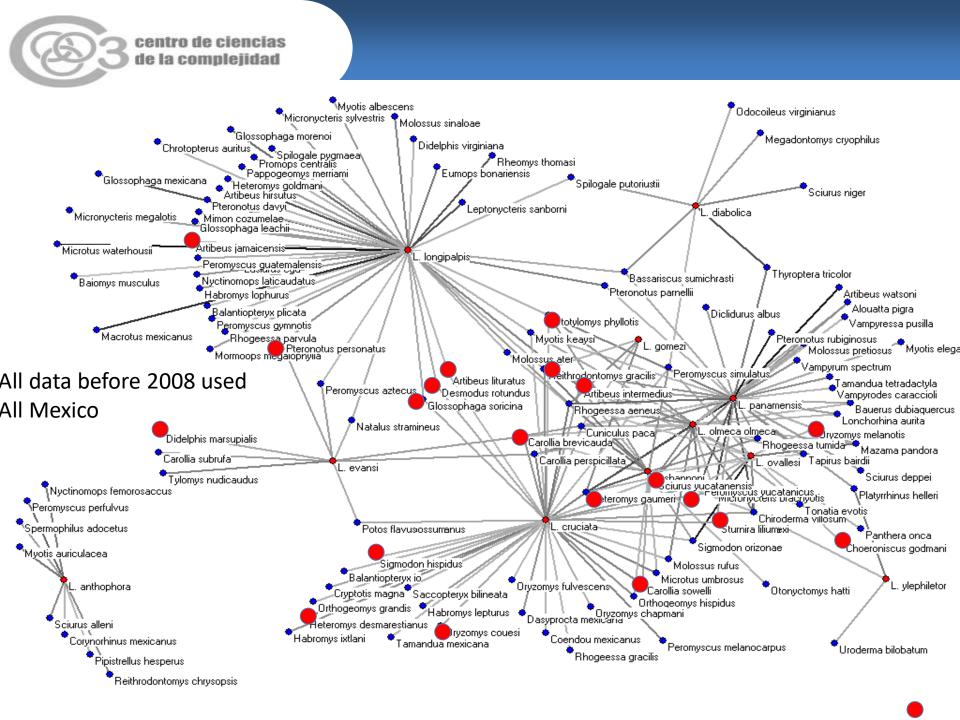


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105 \ 106 E 107 L 108 C 109 L 110 F 111 F 112 A 113 F 114 E 115 S 116 S 117 L 117 L 118 L 119 F	Vampyrodes caraccioli Eptesicus furinalis Liomys pictus Glossophaga commissaris Lonchorhina aurita Phyliostomus discolor Peromyscus gymnotis Anoura geoffroyi Platyrrhinus helleri Eumops bonariensis Sciurus variegatoides Uroderma bilobatum Lasiurus intermedius	3.6929 3.6453 3.6107 3.4861 3.4781 3.4781 3.4781 3.4516 3.4201 3.3586 3.3398 3.3398 3.3398		
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107 L 108 C 109 L 110 F 111 F 112 A 113 F 114 E 115 S 116 L 117 L 118 L 119 F	Liomys pictus Glossophaga commissaris Lonchorhina aurita Phyllostomus discolor Peromyscus gymnotis Anoura geoffroyi Platyrrhinus helleri Eumops bonariensis Sciurus variegatoides Uroderma bilobatum Lasiurus intermedius	3.6107 3.4861 3.4781 3.4781 3.4516 3.4201 3.3586 3.3398 3.3398 3.3373		
108 ( 109 L 110 F 111 F 112 / 113 F 114 E 115 S 116 L 117 L 118 L 119 F	Glossophaga commissaris Lonchorhina aurita Phyliostomus discolor Peromyscus gymnotis Anoura geoffroyi Platyrrhinus helleri Eumops bonariensis Sciurus variegatoides Jroderma bilobatum Lasiurus intermedius	3.4861 3.4781 3.4781 3.4516 3.4201 3.3586 3.3398 3.3398 3.3373		
109 L 110 F 111 F 112 / 113 F 114 E 115 S 116 L 117 L 118 L 119 F	Lonchorhina aurita Phyllostomus discolor Peromyscus gymnotis Anoura geoffroyi Platyrrhinus helleri Eumops bonariensis Sciurus variegatoides Uroderma bilobatum Lasiurus intermedius	3.4781 3.4781 3.4516 3.4201 3.3586 3.3398 3.3398 3.3398 3.3373		
110 F 111 F 112 / 113 F 114 E 115 S 116 U 117 L 118 L 119 F	Phyllostomus discolor Peromyscus gymnotis Anoura geoffroyi Platyrrhinus helleri Eumops bonariensis Sciurus variegatoides Uroderma bilobatum Lasiurus intermedius	3.4781 3.4516 3.4201 3.3586 3.3398 3.3398 3.3373		
111 F 112 / 113 F 114 E 115 S 116 U 117 L 118 L 119 F	Peromyscus gymnotis Anoura geoffroyi Platyrrhinus helleri Eumops bonariensis Sciurus variegatoides Uroderma bilobatum Lasiurus intermedius	3.4516 3.4201 3.3586 3.3398 3.3398 3.3373		
112 / 113 F 114 E 115 S 116 L 117 L 118 L 119 F	Anoura geoffroyi Platyrrhinus helleri Eumops bonariensis Sciurus variegatoides Uroderma bilobatum Lasiurus intermedius	3.4201 3.3586 3.3398 3.3398 3.3373		
113 F 114 E 115 S 116 U 117 L 118 L 119 F	Platyrrhinus helleri Eumops bonariensis Sciurus variegatoides Jroderma bilobatum Laslurus intermedius	3.3586 3.3398 3.3398 3.3373		
114 E 115 S 116 U 117 L 118 L 119 F	Eumops bonariensis Sciurus variegatoides Uroderma bilobatum Lasiurus intermedius	3.3398 3.3398 3.3373		
115 S 116 U 117 L 118 L 119 F	Sciurus variegatoides Uroderma bilobatum Lasiurus intermedius	3.3398 3.3373		
116 L 117 L 118 L 119 F	Uroderma bilobatum Lasiurus intermedius	3.3373		
117 L 118 L 119 F	asiurus intermedius			
118 L 119 F		3.2197		
119 F		3.1739		
	Peromyscus megalops	3.1410		
120 F	Eumops glaucinus	3.0564		
	Urocyon cinereoargenteus			
	Procyon lotor	2.9502		
	Hylonycteris underwoodi	2.9343		
	Rhynchonycteris naso	2.8580		
	Eptesicus brasiliensis	2.8106		
	Myotis albescens	2.8106		
	_ophostoma evotis	2.8106		
	Tapirus bairdii	2.8106		
	Vampyrum spectrum	2.8106		
	Marmosa mexicana	2.7731	Yes	
	Peromyscus furvus	2.7731	100	
	Myotis velifera	2.5757		
	Spilogale putorius	2.5411		
	Microtus mexicanus	2.5268		
	Dasypus novemcinctus	2.4725		
	Myotis nigricans	2.4704		
	ophostoma brasiliense	2.4407		
	Diclidurus albus	2.4407		
	Sciurus niger	2.4407		
	Leptonycteris curasoae	2.4407		
	Nyctomys sumichrasti	2.4026		
	Sigmodon mascotensis	2.3815		
	Alouatta pigra	2.3374		
	Peromyscus melanophrys	2.2204		
	Dermanura tolteca	2.1920		
	Trachops cirrhosus	2.1663		
	Bauerus dubiaquercus	2.1603		
	Spilogale pygmaea	2.1612		
	Leptonycteris nivalis	2.1612		
	Sylvilagus floridanus	2.1402		





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## **Modelling Works!**

- Predicted and confirmed 21 new species of mammal as carriers of Leishmania in Mexico (about 30% of those tested)
- 12 of them are bats, identified for the first time in Mexico
- Squirrels identified as carriers
- Changes the picture for control of Leishmania totally; Leishmania and Lutzomyias are eclectic in their host source. Linnean classification is NOT ecologically relevant
  - So we can see that the biotic (mammals/food)part of the Niche Space for Leishmaniasis is important. What about other factors?
    - Abiotic Worldclim
    - Vegetation/landcover

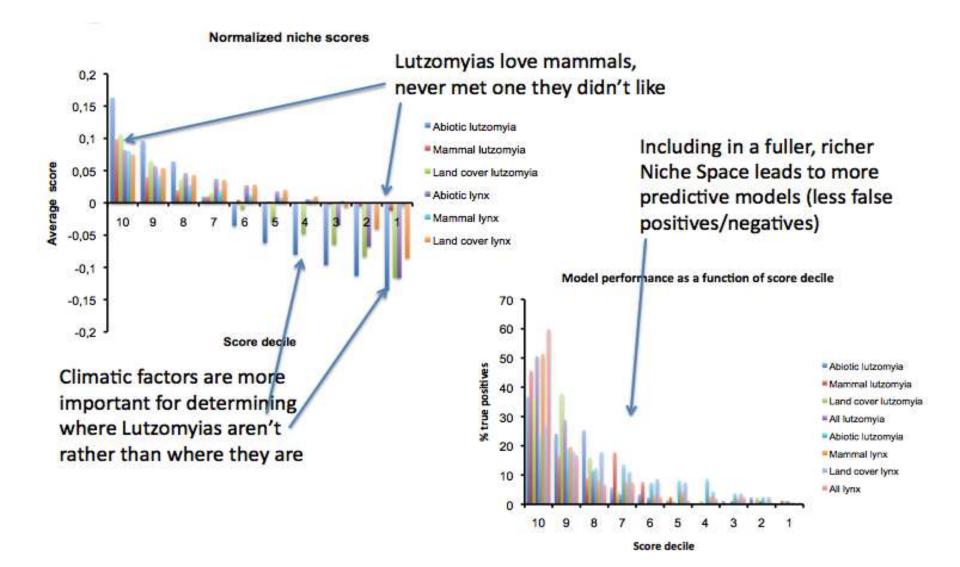


### Modelling the Niche Space of Leishmaniasis (well, Lutzomyias really)

TOP DECILE Optimal niche conditions for Lutzomyia			BOTTOM DECILE Suboptimal niche conditions for Lutzomyia				
ABIOTIC VARIABLE	S RANGE	Epsilon	Score contribution	ABIOTIC VARIABLES	RANGE	Epsilon	Score contribut
BI017	88-219	8.960	5.013	BIO12	42-507	-5.604	-2.279
BIO1	23.3-26.4	8.938	1.006	BIO16	18-218	-5.001	-2.328
BIO11	22.2-25.3	8.873	2.322	BIO18	1-249	-3.839	-3.799
BIO14	26-63	8.782	4.916	B106	3.1-3.4	-3.761	-2.931
BIO4	25.35-33.09	7.543	2.152	BI07	26.3-28.4	-3.544	-8.853
BIO6	13.4-16.6	7.524	3.293	BI02	16.5-18.4	-3.535	-2.997
BIO13	392-774	7.107	12.913	BI011	2.9-12.5	-3.271	-4.482
BI07	28.5-30.6	7.012	3.803	BI04	3310-7184	-2.971	-9.551
BIO16	1019-2019	6.925	12.175	BIO19	192-383	-2.940	-0.448
BIO19	192-383	6.618	4.157	BIO10	28.9-32.3	-2.669	-0.916
BIO12	1906-3302	6.314	8.701	BIO1	10.3-19.9	-2.189	-1.033
BIO2	9.8-10.8	6.130	4.458	BIO3	3.7-5.5	-2.130	-3.576
BIO18	623-746	5.748	1.260	BIO8	28.4-31.7	-1.964	-0.731
RESERVOIRS		511.10		and the second se	RVOIRS		
Reithrodontomys gra	cilis	8.892	2.640	Sigmodon hispidus		6.946	1.244
Heteromys gaumeri	948 	8.800	2.234			6802020	0,143,840
Heteromys desmares	tianus	8.716	2.381				
Ototylomys phyllotis		7.559	2.028				
Peromyscus yucatan	icus	7.249	2.116				
Sigmodon hispidus		6.946	1.244				
Didelphis marsupialis		5.774	1.662				
Oryzomys melanotis	5	3.494	1.387				
Marmosa mexicana		2.773	1.541				
the second s	ND COVER		1012250	LAND	COVER		
Cloud forest		6.642	1,408	Subtropical scrub	and Tables	-1.675	-1,527
Tropical evergreen fo	rest	6.603	4.476			-1.849	-1.658
Cloud forest with sec		6.028	1.459	The second se		-2.092	-3.640
	rest with secondary vegetation	6.007	4.344			-2.924	-4.044
Agriculture areas	tost managedondary regolation	5.966	1.736			-3.337	-1.714
Human settlement		4.947	0.577	Grassland		-3.734	-1.874
100000000000000000000000000000000000000	rest with secondary vegetation	4.081	1.013	Mangroves		-4.063	-2.000

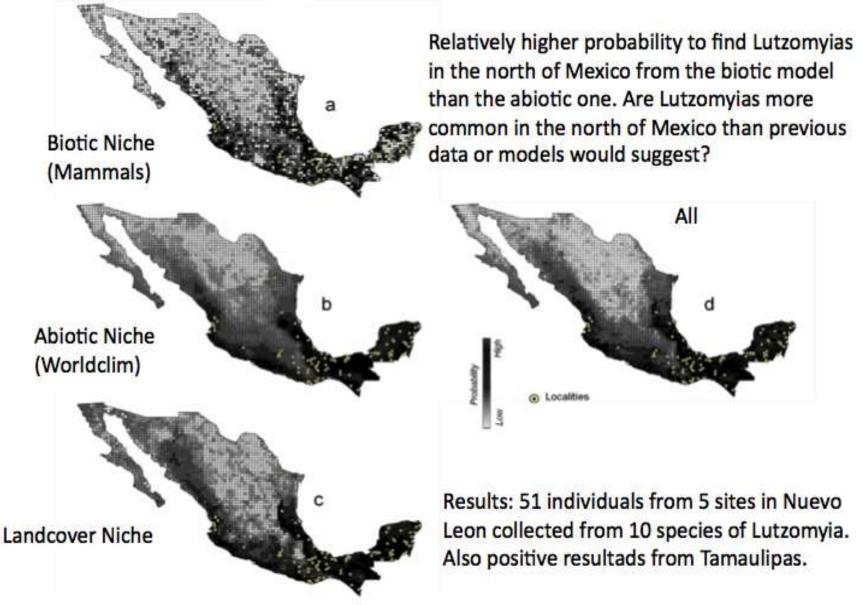


### Modelling the Niche Space of Leishmaniasis (well, Lutzomyias really)



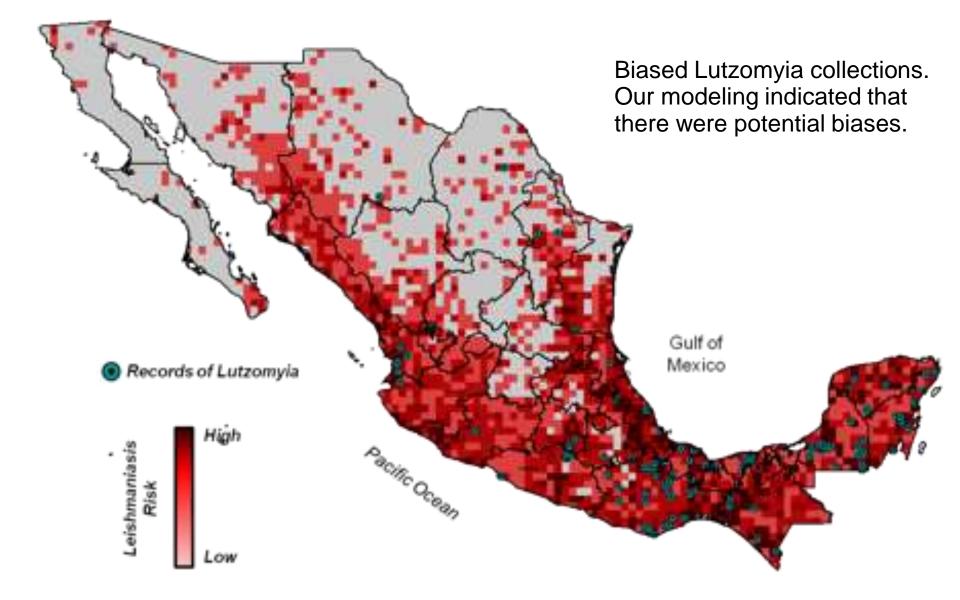


### Lutzomyia Risk Maps from Different Niche models



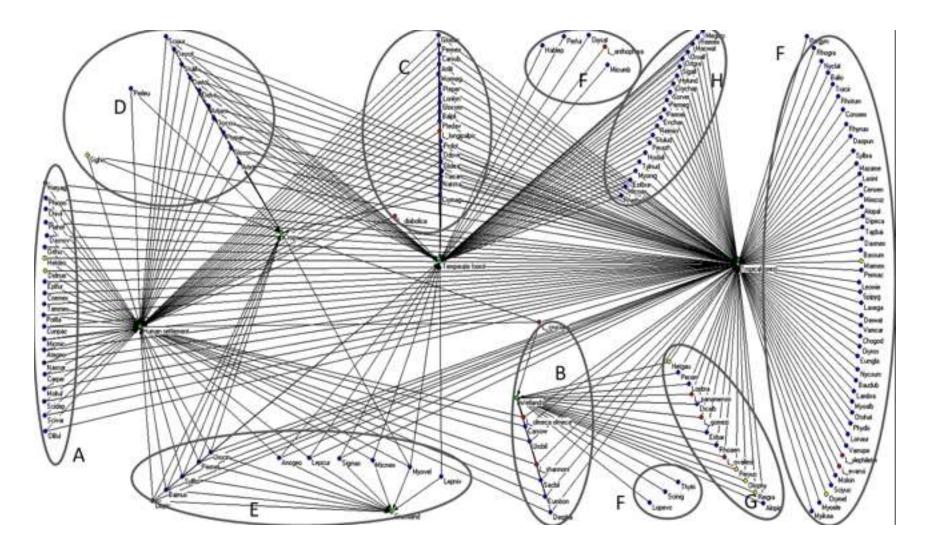


### Lutzomyia Risk Maps from Mammals and Landcover



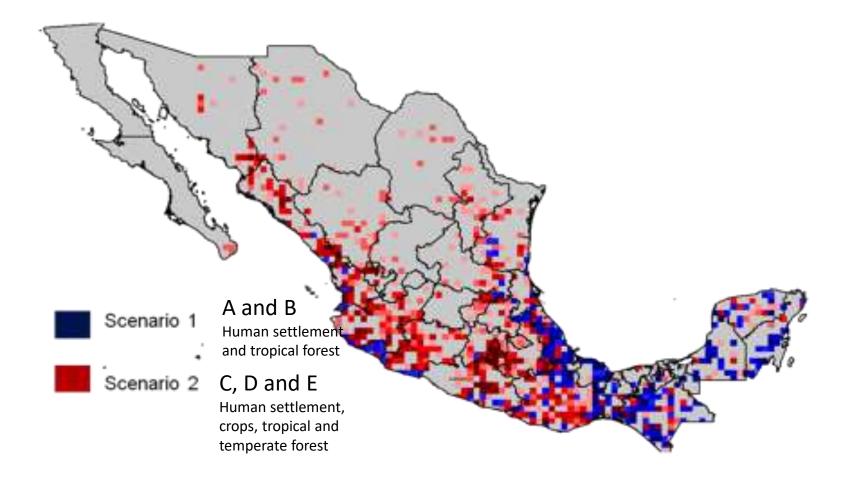


Making the Network more complex: Potential patterns of dispersal



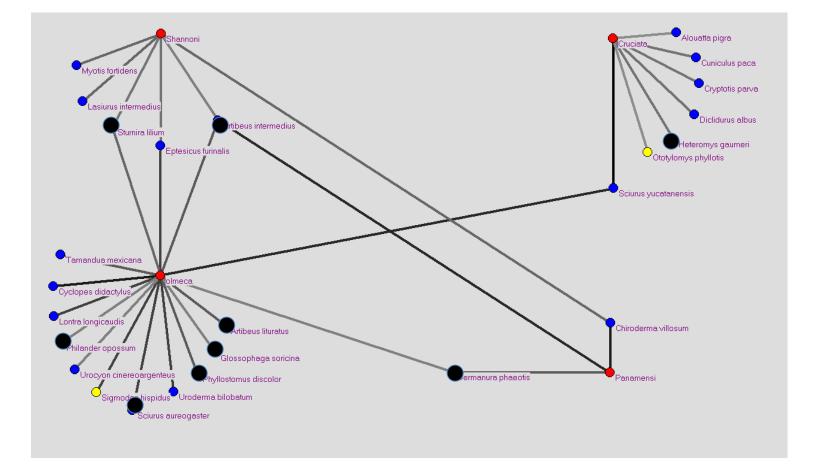


#### **Generating dispersal scenarios**





Drilling down to a more local level... The biotic network for Tabasco



C. Gonzalez, Universidad de los Andes, Bogota



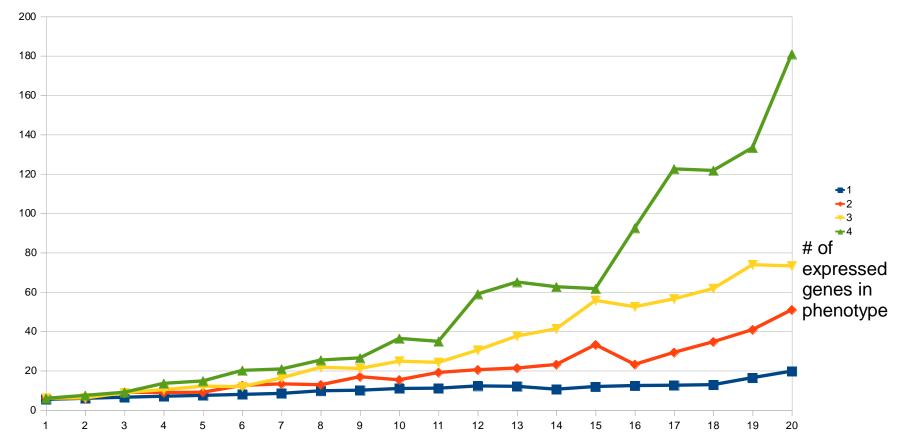
# And now from macro to micro...

# How do pathogens manage to thrive in a large range of hosts?

How do they generate and maintain phenotypic diversity?



#### Infection lifetime



Mutation rate



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# Conclusions

#### **Emerging zoonoses are complex SYSTEMS**

- They are also composed of complex SUB-SYSTEMS
- Many variables are relevant and the micro and the macro are intimately related
- Their study requires potentially large, interdisciplinary teams

We CANNOT do "science" (separate, controlled experiments) to determine the effect of every variable (No PV=RT)

#### The world is awash with data

- Much of this data can be used to (indirectly) infer interactions/relationships/risk factors
- E.g. Predicting the distribution of Lutzomyia, a model with about 500 variables, using point collection data
- Inference networks are a great way of understanding and visualising potential biotic/abiotic/other interactions



# Conclusions

#### **A Modeling at a true systems level IS possible**

Difference between prediction and understanding

Correlation versus causation

Phenomenological versus "fundamental" models

# **Relevant Publications**

Stephens, Christopher R., et al. "Using biotic interaction networks for prediction in biodiversity and emerging diseases." *PloS one* 4.5 (2009): e5725.

González-Salazar, C., and C. R. Stephens. "Constructing Ecological Networks: A Tool to Infer Risk of Transmission and Dispersal of Leishmaniasis." *Zoonoses and Public Health* 59.s2 (2012): 179-193.

Sánchez-Cordero, Víctor, et al. "Competitive interactions between felid species may limit the southern distribution of bobcats Lynx rufus." *Ecography* 31.6 (2008): 757-764.

González-Salazar, Constantino, Christopher R. Stephens, and Pablo A. Marquet. "Comparing the relative contributions of biotic and abiotic factors as mediators of species' distributions." *Ecological Modelling* 248 (2013): 57-70.