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CARACTERIZACION DE REDES Y METACOMUNIDADES VIRALES ASOCIADAS A ROEDORES Y QUIRÓPTEROS

TESIS

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"La materia no sólo interactúa, también se organiza. Conocemos básicamente todas las leyes de interacción de la materia, pero no sabemos casi nada sobre sus leyes de organización."
Albert L. Lehninger (1917-1986)

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Resumen

Los murciélagos son reconocidos como reservorios de enfermedades que han tenido gran impacto en la humanidad. Por lo que se manifiestan interrogantes sobre sus características intrínsecas que les permiten ser tan buenos reservorios de dichos virus. Además, estos virus también tienen “facilidad” para adaptarse a otras especies, incluidos los humanos. Para reconocer dichas características de las asociaciones virus-murciélago deben ser comparadas con asociaciones similares como lo son virus-roedor, mamíferos similares a ellos, por su ancestría, diversidad e historias de vida. Se construyó una base de datos de los virus que se han asociado a dichos hospederos, es decir, secuencias virales detectadas en diferentes tipos de muestras tomadas de los hospederos, y de esta manera implementar la Teoría de Metacomunidades y la Teoría de Grafos para reconocer las diferencias entre las asociaciones virus-murciélago y virus-roedor. Con la Teoría de Metacomunidades se calculó el recambio, anidamiento y agrupamiento para cada una de las escalas (Continental, Biogeográfico, Zoogeográfico y Regional) y taxonómicas (familia y especie viral) para clasificarlas en la estructura correspondiente conforme al árbol de decisiones de Presley. Se detectaron las estructuras cuasi Clementsiana, Clementsianas y aleatorias, siendo estas últimas en mayor número. Posteriormente se realizó un análisis de Ordenación Canónica comparando las variables explicitarías filogenéticas y funcionales (masa corporal, tamaño de camada, camadas por año y gremio trófico). Donde se observó que la expresión predominante de características filogenéticas y/o funcionales de es dependiente a la región y escala analizada. Sugiriéndonos la historia natural y los procesos de adaptación tanto de los patógenos como de los hospederos en cada escala. Por otro lado, con la teoría de Grafos se construyeron redes de asociación virus-hospedero, resaltando si son zoonoticos y añadiendo al humano para reconocer sus agrupamientos y por lo tanto su potencial zoonotico. Se reconocieron las diferencias en la capacidad asociativa de los virus con sus respectivos hospederos al calcular métricas de centralidad de la red para cada nodo (grado, intermediación y centralidad). Encontramos que Gbagrouvirus y Parvovirus del Murciélago Frugívoro deben ser monitoreados por su potencial zoonotico. Además, con ambas teorías se observó que los roedores tienen asociaciones uno a uno. En cambio los murciélagos comparten en mucho mayor grado los virus, siendo esta una de las características que los hacen mejores reservorios. El entender estas características que los diferencian y las reglas de asociación virus-hospedero, nos ayuda a tomar decisiones en vigilancia y control epidemiológico e incluso en la predicción de la distribución y diseminación viral.

Palabras clave: Zoonosis, Epidemiología, Ecología de Enfermedades, Meta-análisis, Gbagrouvirus, Parvovirus del Murciélago Frugívoro.

Abstract

Bats are recognized as good reservoirs of diseases with high impact in humans. For that reason, we ask us about their characteristics which ones give them the capability to do reservoirs of virus and an easy human transmission. To recognize the characteristics of virus-bat association, they must be compared whit similar associations as virus-rodent. Rodents are mammals similar to bats by their ancestry, diversity and life histories. A data base was build with virus associated to bats and rodents, that is to say, viral sequences detected over different type of samples. We analyzed with Metacommunity Theory and Graphs Theory to recognize the differences between virus-bat and virus-rodent associations. With Metacommuity Theory, it estimated returned, nested and clustering in each scale (Continental, Biogeographic, Zoogeographic and Regional) and taxonomical (family and viral specie) to classify by their structure, using Presley´s Decisions

Tree. We detected Quasi-Clementsian structures, Clementsian and Random structures. After that, we did an Ordination Canonical Analyze to compare explanation variables: phylogenetic and functional (body mass, litter size, litters per year and trophic guild). We observe the predominant expression of phylogenetic or functional characteristics depending of the region and scale analyzed. The structures suggest us natural histories and adaptation process of the pathogens and also of hosts in each scale. Besides, whit the Graphs Theory, we constructed association networks virus-host, highlighting zoonotic viruses and added the human to recognized their grouping and their zoonotic potential. We recognized associative differences between their hosts when we calculated centrality metrics for each node (degree, betweenness and closeness). We found potential zoonotic in Gbagrouvirus and Fruit Bat Parvovirus and they will be monitored. Also, with both theories, we found the different association, because rodents have associations one to one, but bats share virus in a high degree, given them the capability to do better reservoirs. Understand the characteristics that difference and association rules virus-host, we can take better decisions in epidemiological surveillance and control, and also in viral distribution and dissemination.

Índice

Contenido

Introducción

Los murciélagos y los roedores son hospederos de una proporción significativa de zoonosis, mayor a las de cualquier otro orden de mamíferos, con un reporte de 25 zoonosis únicas para murciélagos y 85 para roedores (Han, Kramer, & Drake, 2016; Olival et al., 2017). Pero Olival et al. (2017) mencionan que los murciélagos tienen una mayor proporción de zoonosis cuando se estandariza el esfuerzo de muestro.

En total, se han reportado más de 200 virus aislados o detectados sobre murciélagos. Estos virus están categorizados en 27 familias virales y se observaron sobre 11 familias de murciélagos. Sin embargo, debemos tomar en cuenta que no todos los virus son patógenos, algunos de ellos se han co-adaptado con sus hospederos.

Históricamente, el primer virus aislado de los murciélagos fue el virus de la rabia. El virus de la rabia es de gran relevancia por su mortalidad al humano, al ganado, a los animales de compañía y a otros vertebrados. Pero esta capacidad mortal del virus de la rabia es cuestionable al infectar a los murciélagos, ya que, se propone que los murciélagos fungen como portadores asintomáticos del virus. Este tema es controversial por la carencia de pruebas en cualquiera de las direcciones (Wang & Crowled, 2015).

Pero la rabia no es el único virus con relevancia en salud pública que se ha detectado con métodos moleculares o serológicos sobre los murciélagos. Dentro de ellos podemos mencionar al Hendra virus que es reconocido en 1994 sobre caballos y sobre dos humanos. Posteriormente se identifica en los zorros voladores y murciélagos frugívoros (*Pteropus alecto, P. poliocephalus* y *P. conspicillatus*) exponiéndolos como reservorios naturales del virus (Young et al., 1996).

En 1998, en Malasia, se reportaron cerdos con enfermedad neurológica y respiratoria que se asoció a una encefalitis febril aguda frecuentemente mortal en humanos. Posteriormente se reconoce el agente etiológico y es nombrado como Nipa virus. Al analizar el Nipa virus detectan gran similitud con el Hendra virus, por lo tanto se enfocan en los murciélagos como reservorios naturales. Al buscar estos virus en los murciélagos, encuentran anticuerpos en un gran número de murciélagos de Malasia, India y Bangladesh (O'Shea et al., 2014; Plowright et al., 2015; Wang & Crowled, 2015).

Un año después, en 1999 se detecta el virus Marburg en muestras de murciélagos *Rousettus aegyptiacus, Rhinolophus eloquens* y en *Miniopterus inflatus* en la Republica del Congo (Pourrut et al., 2009). Dentro de la misma familia filoviridae, en el 2014, se registro la más grande epidemia de Ebola con más de 10,000 casos confirmados y miles de muertes. Como reservorios del virus Ebola se detectaron a los murciélagos frugívoros e insectívoros (Allocati et al., 2016).

Los murciélagos tienen una gran diversidad de coronavirus y probablemente son el reservorio natural y ancestral de los alfacoronavirus y betacoronavirus. Se sabe que los virus se adaptan a otras especies animales y los coronavirus no han sido la excepción (Wang & Crowled, 2015). Dentro de los coronavirus zoonoticos más importantes se encuentra el SARS coronavirus y el MERS coronavirus. Ambos altamente patogénicos al humano, con altas tasas de mortalidad (Anthony et al., 2017; Hu, Ge, Wang, & Shi, 2015).

Con el anterior historial de virus emergentes y de alto impacto en la población humana, se manifiestan interrogantes sobre las características intrínsecas de los mismos, ¿qué es lo que les permite ser tan buenos reservorios de dichos virus y su “facilidad” para que los humanos adquieran estos virus? (Moratelli & Calisher, 2015).

Se han realizado varias propuestas para resolver la interrogante, principalmente debemos reconocerlos como el único mamífero con la capacidad de volar y ecolocalizarse dejándolo casi libre de depredadores y competidores (Wang & Crowled, 2015).

El tener la capacidad de volar, promueve una traslación más amplia (alrededor de 10 km para los sedentarios), e incluso adquieren la habilidad de migrar. A pesar de que menos del 7% de los murciélagos tienen esta capacidad de migrar, el impacto es amplio, ya que pueden volar desde cientos o hasta 2000 km de distancia, lo cual facilita la diseminación viral (Hutterer, 2005; Wang & Crowled, 2015).

Por si fuera poco con relación al vuelo, se presenta la hipótesis de que el vuelo funge como presión selectiva a los virus para co-existir con tasas metabólicas elevadas y temperaturas febriles, reacciones que son naturales del organismo de los mamíferos como defensa a las infecciones virales (O’Shea et al., 2014).

Otra característica sobresaliente del orden chiroptera es su diversidad y distribución, ya que son el segundo orden más diverso con 1301-1331 especies descritas (Wang & Crowled, 2015) y están distribuidos alrededor de todo el mundo a excepción de los polos y algunas islas (Rydell, 2009).

También cuentan con una gran diversidad de dietas, desde nectarívoros, frugívoros, insectívoros, omnívoros y carnívoros. Esto facilita el contacto con un mayor número de virus, desde los arbovirus con los que las tasas de contacto se incrementan con los murciélagos insectívoros, hasta el Ebola virus con el cual se propone su adquisición al consumir fruta (Luis et al., 2015).

Otra característica propia de los murciélagos es su esperanza de vida que es 3.5 veces mayor que la de otro mamífero terrestre placentado de una talla similar (Wang & Crowled, 2015). Esto le permite tener contacto y recabar una mayor diversidad viral a lo largo de su vida.

Por si fuera poco, también tienen una alta plasticidad en cuanto a los sitios en donde pueden refugiarse, desde cuevas, árboles, casas abandonadas, entre otros sitios (Wang & Crowled, 2015). Por lo tanto, tienen la habilidad de adaptarse a sitios antropizados e incluso encontrar refugio dentro de las ciudades.

Equiparables a los murciélagos y como se había mencionado, con similar potencial zoonotico, se encuentran los roedores. Se les atribuyen diversos virus zoonoticos y dentro de ellos el más reconocido por su impacto en la población humana es el Hantavirus. Al año, se diagnostican 100,000 casos de Hantavirus en Asia. En 1993, se le atribuyó un 50% de mortalidad en el sureste de EUA (Mills, 2006; Nichol et al., 1993).

Dentro del mismo grupo de los Hantavirus se encuentra el virus Sin Nombre que se distribuye principalmente en el Norte de América y se reconoce a *Peromyscus maniculatus* como principal reservorio. En cambio el principal distribuidor de Hantaan virus en China, Rusia y Corea es *Apodemus agrarius*. Por lo que podemos concluir que los anteriores roedores fungen como dispersores regionales (Meerburg, Singleton, & Kijlstra, 2009; Mills, 2006) y como dispersores mundiales del virus Seoul se reconoce a *Rattus norvegicus* y *Rattus rattus*.

Otro Hantavirus es Pumala virus, asociado a *Myodes glareolus* y *Myodes rufocanus,* zoonosis que tiene una tasa de 1% de mortalidad (Meerburg et al., 2009; Mills, 2006). En general, los Hantavirus son responsables de entre 60,000 a 150,000 casos de humanos hospitalizados con un rango de mortalidad entre el 5% y 10%.

Dentro de la familia viral *Bunyaviridae*, la fiebre hemorrágica del Congo afectó a más de 3,400 humanos durante los 1940´s y se ha reconocido como reservorios a diversas especies de roedores, sobre los cuales se detectaron anticuerpos (Meerburg et al., 2009).

En los 1950´s se descubrió la enfermedad de la selva de Kyasanur que afectaba entre 100 a 500 personas al año con una mortalidad entre 2% y 10% (Gould & Solomon, 2008) el cual también está asociado a *Rattus rattus* como reservorio (Meerburg et al., 2009).

Con distribución en Rusia, Europa, China y Escandinavia, la encefalitis por garrapata es responsable de 11,000 casos de infección anuales en Rusia y 3,000 en el resto de Europa. (Gritsun, Nuttall, & Gould, 2003) y puede resultar mortal o con secuelas neuropsiquiatricas (Meerburg et al., 2009).

Los arenavirus también están relacionados con los roedores, por ejemplo, la Fiebre de Lassa, que se distribuye en el Oeste de África y se estiman entre 100,000 a 300,000 infectados con aproximadamente 5,000 muertes (Khan et al., 2008) y su principal reservorio es *Mastomys natalensis* (McCormick et al., 1986).

En los 1990´s se reconoce el virus Tamiami que fue encontrado en *Sigmodon hispidus* y no fue, sino hasta 1996 cuando se detecta en *Neotoma albigula* en Nuevo México (Meerburg et al., 2009).

Los roedores también son reservorios del virus de la Encefalitis Equina Venezolana asociado principalmente a el roedor *Sigmidon hispidus* y son reservorios del virus de la hepatitis E. Este ultimo virus se encuentra asociado al género Rattus con una prevalencia de anticuerpos de hasta 59.7% (Meerburg et al., 2009).

Con los virus anteriormente mencionados, podemos observar lo equiparables que son los roedores con los murciélagos, pero no solo en su potencial zoonotico sino también en sus historias de vida como se explicará adelante:

Los roedores son el orden más diverso de la clase mammalia con aproximadamente 2280 especies descritas (Fowler & Cubas, 2001) por lo que representan cerca del 43% del número total de mamíferos (Huchon et al., 2002; Meerburg et al., 2009). Son mamíferos cosmopolitas que habitan en todos los continentes exceptuando la Antártica (Fowler & Cubas, 2001; Meerburg et al., 2009)

Similar a los murciélagos tienen una dieta diversa, desde hierbas, semillas hasta carne. Pero cabe resaltar que compiten por el alimento con los humanos, es decir, los roedores son una plaga común de los cultivos, lo que incrementa el contacto y asociación que tienen con los humanos y su alimento. Este alimento puede tener contacto con excreciones de los roedores e infectar al humano al consumirlo.

Una característica destacada del orden Rodentia es su alta tasa de fecundidad y su intervalo generacional corto, esto genera poblaciones con altas densidades que elevan las prevalencias virales, fomentan la dispersión de los roedores y por ende facilitan el contacto con el humano (Meerburg et al., 2009).

En cuanto a su hábitat se sabe que los roedores que están asociados a virus altamente zoonoticos son especies generalistas que logran adaptarse a diferentes entornos. Estos roedores logran adaptarse a sitios altamente antropizados. Como se mencionó anteriormente, se adaptan a sembradíos por el acceso al alimento, además de que podemos encontrarlos en almacenes, edificios e incluso en nuestras casas y jardines (Mills, 2006).

En general observamos que ambos órdenes tiene alto potencial zoonotico y comparten características como su capacidad adaptativa a sitios antropizados y su riqueza tanto de especies, como viral. Pero también cada uno cuenta con características propias que indirectamente le permiten explotar este potencial de manera diferente, como lo es el vuelo o las poblaciones con altas densidades, por mencionar solo algunas.

Sin embargo, se ha observado una mayor atención y estigmatización hacia los murciélagos, probablemente por la rapidez con la que han surgido los saltos de hospedero (Allocati et al., 2016; Brook & Dobson, 2015; Calisher, Childs, Field, Holmes, & Schountz, 2006). Esto se observa fácilmente al comparar los años en que han sido descubiertos los virus en cada uno de los órdenes.

Esta diferencia de años no solo influye en el intervalo neto, sino también el tiempo de adaptación y convivencia que ha tenido el humano con estos virus y aun más importante, el contexto tecno-científico en el que están inmersos. Es decir, el avance de la biología molecular ha permitido rastrear estos virus a una velocidad impresionante que nos ha llevado a sus reservorios naturales.

Debemos tomar en cuenta que el potencial zoonotico se ha evaluado con el número absoluto de simbiontes zoonoticos dentro de cada género (Han et al., 2016) y debemos reconocer que existen una serie de pautas que facilitan los saltos de hospedero y se abordan de manera diferente entre las especies (Plowright et al., 2015).

Tenemos claro que los órdenes son diferentes y con reporte de alto potencial zoonotico, pero vamos a reconocer si sus diferencias son destacables, ya que al involucrar características filogenéticas y funcionales, la naturaleza de sus asociaciones virus-hospedero son distintas; de tal modo que su potencial zoonotico sea diferente al que se puede obtener con un conteo de virus detectados.

Una manera de responder estas interrogantes es con la aplicación de la Teoría de Metacomunidades la cual nos refiere el contexto ecológico en el que se están llevando a cabo estas asociaciones y la influencia de las características filogenéticas y funcionales. Que es corroborada y complementada con la Teoría de Grafos la cual nos resalta las conexiones directas virus-hospedero que facilitan los saltos de hospedero por cumplir la primer pauta que se refiere al contacto entre especies (Plowright et al., 2015).

El presente proyecto utiliza estas dos herramientas con el objetivo general de reconocer las características en las asociaciones virus-hospedero que les ofrecen la capacidad de ser mejores reservorios y potencializan su capacidad zoonotica. El cual se presenta en tres capítulos:

Capítulo I.- Revisión de la Teoría de Metacomunidades y la Teoría de Grafos. Donde se explican las bases teóricas de cada una de las teorías para aplicarlas en los análisis posteriores.

Capítulo II.-La Teoría de Metacomunidades: con el objetivo de reconocer las características filogenéticas y funcionales a las que responde la organización de las metacomunidades a diferentes escalas geográficas y taxonómicas. Obteniendo resultados con un enfoque ecológico, es decir reconociendo la historia natural de los procesos de adaptación tanto de los patógenos como de los hospederos.

Capítulo III.- La teoría de Grafos: con el objetivo de reconocer las diferencias en la capacidad asociativa de los virus con sus respectivos hospederos. Que, en este caso, se obtiene un mayor enfoque epidemiologíco al resaltar las asociaciones entre virus zoonoticos-no zoonoticos y sus hospederos incluyendo al humano y así detectar virus próximos a él.

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Capítulo 1. Revisión de la Teoría de Metacomunidades y la Teoría de Grafos.

Introducción

Las enfermedades que afectan a la fauna silvestre reducen o extinguen poblaciones. Esto provoca que se rompan las interacciones de las especies y modifican el funcionamiento del ecosistema. De tal forma que es necesario entender la dinámica de estas enfermedades para proteger los ecosistemas. Las enfermedades son parte del ecosistema, en el cual también ejercen presiones intraespecificas e interespecificas en los seres vivos regulando su diversidad biológica por medio de diferentes mecanismos, algunos aun desconocidos, que dirigen los procesos evolutivos, de especiación y la distribución geográfica de los seres vivos (Suzán Azpiri, Galindo Maldonado and Ceballos González, 2000).

También, debemos estar consientes que estos patógenos forman parte de las dinámicas del planeta Tierra y por lo tanto es imposible erradicarlas sin provocar una cascada de eventos desafortunados para un gran número de especies (Luque, 2008; Beldoménico, Ciencias and Universidad, 2013).

De tal manera, que surge la Ecología de Enfermedades la cual tiene como objetivo entender la dinámica y evolución de las enfermedades con el fin de tomar mejores decisiones en la conservación y protección del ambiente. No obstante su estudio se complica ya que el riesgo y mecanismos de transmisión de la enfermedad puede depender de varias características. Entre las más destacadas se encuentran la diversidad de patógenos presentes en las especies reservorias, es decir, el poliparasitismo o infección múltiple y la dinámica de la infección en los hospederos (Gay *et al.*, 2014).

La ecología de comunidades de enfermedades nos ofrece el marco teórico y las herramientas analíticas para ir más allá en las interacciones parásito-hospedero y considerar todo el juego de especies que influyen en la dinámica de la infección (Johnson, Roode and Fenton, 2016). Cabe destacar que la ecología de comunidades se ocupa de explicar los patrones de distribución, abundancia e interacción de las especies a diferentes escalas espacio-temporales, que debe delimitarse, siendo esta la mayor debilidad, ya que la ecología clásica de comunidades no se enfoca en la dispersión y potencial conexión entre comunidades (Lorencio, 2007); y para poder abarcar esta potencial dispersión de los conjuntos de simbiontes interactuando, es más adecuado considerarlos como una metacomunidad, permitiendo realizar estudios cuando no hay presencia de fuertes barreras geográficas (Suzán *et al.*, 2015).

Las organizaciones, multi-patogeno, multi-hospedero, son aun más complejas, al tomar en cuenta que las enfermedades infecciosas surgen de interacciones entre múltiples especies de hospederos y coexisten con otros simbiontes o parásitos. Estas co-infecciones pueden alterar la patología que presenta el hospedero, la transmisión del parásito y la evolución de la virulencia, ya que el parásito se ve afectado por la condición del huésped, las respuestas inmunitarias, el entorno abiótico y las interacciones con los simbiontes co-infectantes y otros organismos asociados (Johnson, Roode and Fenton, 2016).

A pesar de la existencia de las anteriormente mencionadas presiones de selección para co-evolucionar con sus hospederos, aunadas a procesos de co-especiación que favorecen su diversidad, solo una minoría de patógenos presentan un alto valor de especificidad de hospedero (Woolhouse, 2001).

Por lo que aproximaciones a nivel individual nos ofrecen resultados aislados, también relevantes y que aportan al entendimiento de los sistemas, pero que no toman en cuenta todo el conjunto y no es posible observar propiedades emergentes distintivas de los sistemas complejos. Éstas interrelaciones parásito-hospedero están íntimamente embebidas dentro de comunidades de una gran diversidad de organismos. Por lo que se requiere una comprensión clara del contexto ecológico completo de la infección y transmisión que sólo nos las puede ofrecer aproximaciones multihospedero (Woolhouse, 2001; Suzán *et al.*, 2015; Johnson, Roode and Fenton, 2016). De tal manera que, para reconocer las diferencias entre las asociaciones virus-hospedero se pueden utilizar las herramientas proporcionadas por la teoría de metacomunidades y la teoría de grafos. Ambas aproximaciones nos permiten estudiar la dinámica de asociaciones entre múltiples simbiontes y su diversidad de hospederos.

Teoría de Metacomunidades

Las metacomunidades son un conjunto de comunidades ligadas por procesos de dispersión (Wilson, 1992) de múltiples especies que potencialmente interactúan (Leibold *et al.*, 2004). Estas metacomunidades ocupan una región constituida por sitios, los cuales están distinguidos espacialmente y pueden ser ocupados por un individuo. Cuando se obtiene un conjunto de sitios se constituye un parche que puede ser ocupado por una población o por individuos. Si el parche está ocupado por individuos de varias especies, entonces el conjunto representa una comunidad. Los individuos pueden propagarse, moviéndose entre parches, de esta manera las comunidades quedan enlazadas formando una metacomunidad (Figura 1) (Gonzalez, 2009).

La teoría de metacomunidades nos proporciona algunas herramientas para entender y predecir patrones de biodiversidad; como lo es la variación de la diversidad a diferentes escalas espacio-temporales, estructuras tróficas; la dispersión, colonización y extinción; ligando las interacciones a través de escalas locales y regionales (Leibold *et al.*, 2004; Marcel Holyoak, Mathew A. Leibold, 2005; Miatelo *et al.*, 2007; Gonzalez, 2009; Johnson, Roode and Fenton, 2016).

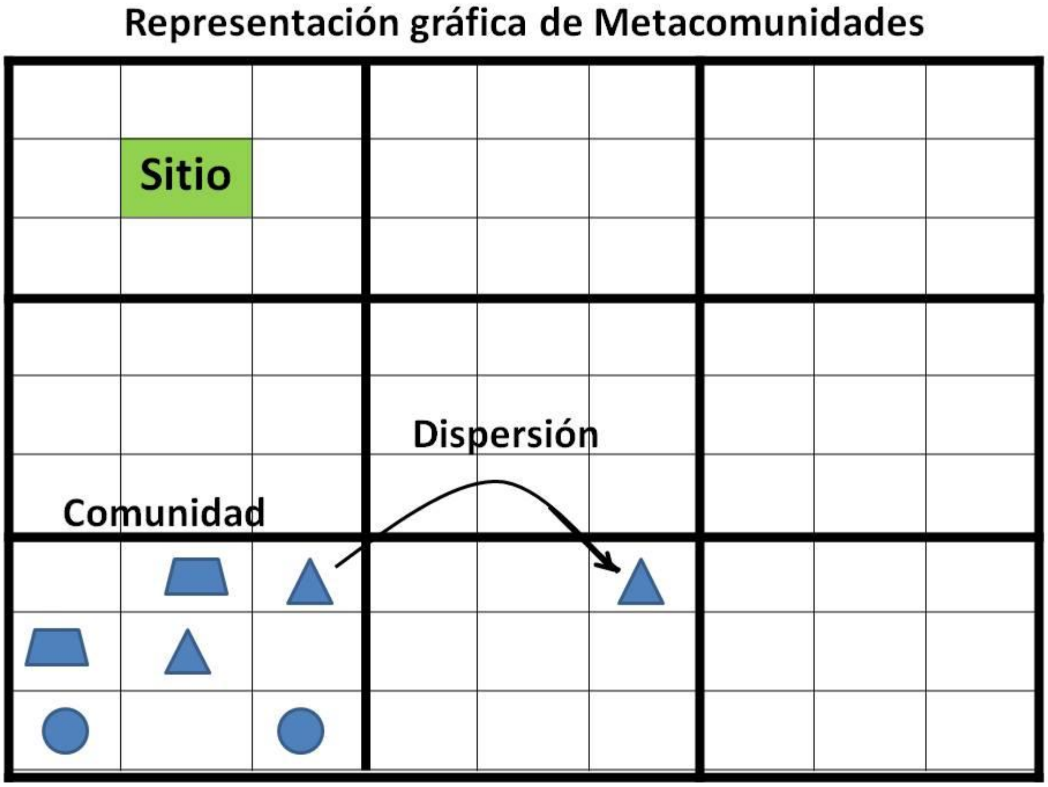


Figura 1.- Representación gráfica de Metacomunidades. Modificada de Gonzalez, 2009.

En el caso de este trabajo, los sitios o parches son representados por los hospederos, los cuales son ocupados por las especies virales y su conjunto conforma una comunidad. Estas comunidades virales se encuentran en constante cambio por la capacidad invasiva o extinción de cada virus. La extinción puede ser ocacionada por la defensa del organismo o la competencia con los demás simbiontes (Mihaljevic, 2012).

Existen 5 modelos sobre metacomunidades (figura 2) que proponen diferentes procesos para explicar la co-existencia de especies. Estas propuestas se deben tomar como modelos complementarios, ya que cada modelo representa procesos que son comunes en la naturaleza y es más pertinente considerar las condiciones bajo las cuales cada uno puede ofrecer una mejor percepción de la realidad (Gonzalez, 2009).

Modelo Neutral

Este modelo supone que las comunidades ecológicas se componen por especies que se comportan como similares. Esta teoría ha generado controversia, ya que sugiere que las diferencias aparentes entre especies no tienen relevancia en la distribución de las especies, es decir, asume que los requerimientos ambientales de las especies son los mismos al igual que sus tasas de colonización y extinción. La principal formulación asume que las especies no son denso dependientes, es decir, independientemente de la densidad poblacional que tenga una especie, ésta se va a distribuir dentro del espacio de igual forma que cualquier otra (Chave, 2004; Hubbell, 2005; Gonzalez, 2009). Podemos imaginar un sitio de muestreo, donde el ambiente es altamente homogéneo y por ende, las especies tienen un nicho similar. Dependiendo de la comunidad a estudiar estas diferencias podrían tender a nulas, como podría ser, dentro de un mismo orden, género o gremio trófico. Sin olvidar el punto de que nos referimos a una zona pequeña de muestreo. Este modelo también asume las mismas tasas de colonización y extinción que puede ser encontrado en comunidades muy especificas con alta señal filogenética, es decir que todos son de un mismo linaje.

En el ámbito de ecología de enfermedades es aun más fácil concebir estos supuestos, sobre todo con simbiontes como lo son los virus, donde encontramos virus tan cosmopolitas como lo es la rabia donde, su limitante de hospederos principalmente es, que pertenezca a la clase Mammalia (OIE, 2008), así de manera sencilla, se puede encontrar una infinidad de hospederos. Dentro de los virus asociados a murciélagos, los coronavirus también se encuentran, en esta clasificación de virus cosmopolitas, fácilmente comparables con la rabia y que dentro de estas escalas pueden comportarse predominante como neutrales.

Modelo de Ordenamiento de especies.

A nivel macroecológico, tomando como referencia países o zonas Biogeográficas, con ambientes altamente heterogéneos podemos encontrar el modelo de ordenamiento de especies. En este modelo se asume que los sitios son altamente heterogéneos. Enfatiza las características del hábitat diferenciando los requerimientos ambientales (nicho ecológico) entre las especies. Las tazas de colonización y extinción de las especies difieren, lo cual afecta las interacciones entre especies (Leibold, 1998; Gonzalez, 2009; Coria, 2014). En este modelo podríamos encontrar especies arraigadas a sus nichos ecológicos y que su dispersión es prácticamente imposible a tan grande escala, como el movimiento de un ajolote a lo largo de un continente. Simbiontes transmitidos por vectores son un ejemplo de comportamientos acorde con este modelo, ya que estrictamente se requiere que tengan contacto los vectores con los hospederos para que la transmisión se lleve a cabo, por lo que limitan su dispersión.

Modelo de Dinámica de Parches

Asume un ambiente físico homogéneo. Los parches o sitios pueden tener dos estados: ocupado o desocupado, simplificando el problema de la representación de abundancias, tomándola como el número de parches ocupados por cada especie. Se asume que la colonización y extinción de las especies están correlacionadas por especie, es decir una especie con baja tasa de colonización tendrá baja tasa de extinción (Cadotte, 2007; Gonzalez, 2009). Si se analiza una superficie mayor, pero que aun conserve su homogeneidad del paisaje, podríamos observar la predominancia de este modelo. Por ser una superficie mayor, es más difícil obtener el número concreto de abundancias, además la diversidad filogenética y funcional se incrementaría, así que las historias de vida de las especies tendrán mayor influencia en su distribución, lo que ayudaría a reconocer especies R de especies K (Landeros *et al.*, 2013). De igual modo, la capacidad de dispersión se ve disminuida ya que la superficie analizada es mucho mayor a su ámbito hogareño. Dentro de este grupo podemos integrar simbiontes con distribución menos masiva y con mayor especificidad, como mejores representantes podemos mencionar a los simbiontes que son transmitidos de manera vertical (The center for food security & public healthsity, 2007).

Modelo de Efecto de Masa

También asume la heterogeneidad ambiental pero introduce la abundancia de las especies y asume altas tasas de dispersión dentro de la metacomunidad. La diversidad es mantenida regionalmente a largo plazo en ausencia de la especiación (Mouquet *et al.*, 2002; Gonzalez, 2009). Este modelo se manifiesta en escalas similares a la anterior o incluso menor, pero que ahora ocupe ambientes heterogéneos. Aquí las especies deben de tener altas tasa de dispersión originando tasas de especiación bajas. En este modelo podemos incluir especies que migran, como las comunidades de aves. Estas aves, pueden habitar en ambientes diferentes y es muy conocida su alta dispersión, donde incluso migran entre zonas biogeográficas (Armesto, Torrado and Llanes, 2013). Curiosamente en el ámbito de simbiontes podemos mencionar a la influenza que por su transmisión por aerosoles facilita la dispersión (JM, MT and Requena, 2006), aunado a que su principal dispersor son las aves que utilizamos como ejemplo para este paradigma.

Modelo de Perturbación-sucesión (del parche)

Como su nombre lo indica enfatiza las perturbaciones y el ciclo de sucesión de las especies. Asume que la colonización por las especies dominantes puede ser facilitada por la presencia de la especie subdominante. La ocupación espacial dentro de cada parche depende de la fuerza de interacción y de las tazas de fecundación, reclutamiento y colonización. Este modelo captura la dispersión abiótica (por corrientes marinas) y la dispersión biótica (tasas de asentamiento dependientes del tiempo) (Guichard *et al.*, 2004; Gonzalez, 2009).

Este modelo es reconocido en las metacomunidades marinas por la influencia que tienen las corrientes marinas en la dispersión de las especies, sin embargo, la superficie terrestre no está excluida de este proceso, ya que en especies principalmente de plantas su dispersión depende de las corrientes de aire. Dentro de las corrientes de aire también están inmersos patógenos, principalmente los que tienen capacidad de esporular. Incluso se han identificado esporas de patógenos en América provenientes de las tormentas de arenas del Sahara(Jorge, 2013).

Estos 5 paradigmas se han presentado como una manera de entender los procesos que determinan la distribución de la diversidad de una forma reduccionista, pero indiscutiblemente necesaria para poder entender los patrones naturales que surgen de la interacción de ellas

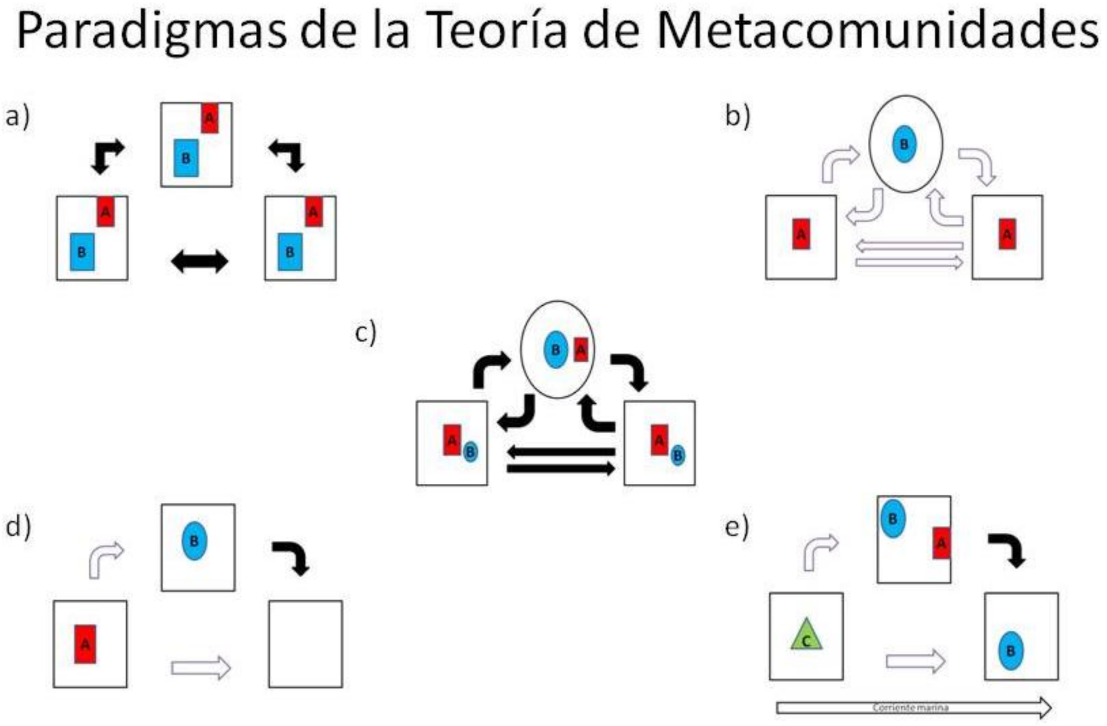


Figura 2 Representación esquemática de los cinco paradigmas de la Teoría de Metacomunidades. Las flechas direccionan la potencial colonización de los sitios por las especies. Las flechas solidas representan una alta dispersión. Los paradigmas ilustrados son: a) neutral, b) ordenamiento de especies, c) efecto de masa, d) dinámica de parches y e) perturbación-sucesión. En a) neutral se observa una distribución homogénea de las especies con igual potencial colonización a los sitios. En b) ordenamiento de especies, la dispersión no es suficiente para alterar sus nichos. En c) efecto de masa, letras pequeñas representan poblaciones más pequeñas. En d) dinámica de parches, se observa que A es mejor competidos pero B es mejor colonizador. En e) perturbación-sucesión, se observa la influencia de las corrientes marinas y A solo puede colonizar sitios con presencia de B. Modificada de (Marcel Holyoak, Mathew A. Leibold, 2005)

Estructuras de las Metacomunidades

Para distinguir entre las 14 estructuras idealizadas de distribución de metacomunidades. Se dividen en 8 estructuras reconocidas por su coherencia significativa y 6 restantes que al no tener coherencia significativa se catalogan como cuasi-estructuras, lo que nos sugiere que están sufriendo un proceso de transformación (Leibold and Mikkelson, 2002). Para detectar la estructura de una metacomunidad se analizan tres elementos: coherencia, recambio y agrupamiento (Leibold and Mikkelson, 2002) y de esta manera determinar en cual encaja y realizar análisis posteriores para establecer el gradiente y su naturaleza (cuadro 1) (Dallas and Presley, 2014).

Coherencia

Para que una estructura de metacomunidad sea coherente se deben cumplir dos requisitos. Primero las ocurrencias de especies deben responder a características ambientales, representando un gradiente de variación ambiental. Segundo, la mayoría de las especies deben responder al mismo gradiente. En caso de no tener coherencia nos indica que las distribuciones no están determinadas por el mismo gradiente ambiental, pudiendo obtener estructuras aleatorias o de tablero de ajedrez (Dallas and Presley, 2014).

Recambio

El recambio es el número de especies que se sustituyen entre las diferentes comunidades que conforman la metacomunidad y es negativo cuando se observa anidamiento. El anidamiento es cuando las especies se van incorporando dentro de otras, es decir se van acumulando las especies. Si el anidamiento es positivo obtenemos estructuras Clementsianas o Gleasonianas, en cambio cuando el recambio es positivo obtenemos estructuras uniformes (Dallas and Presley, 2014).

Agrupamiento

El agrupamiento mide que tan drástico es el cambio de especies entre grupos. Los bordes de la distribución de las especies pueden ser suaves a los largo del gradiente conformando un gran grupo o se pueden separar bruscamente entre ellos.

Se pueden distinguir tres subgrupos anidados; con pérdida de grupos de especies en estructuras Clementsianas, perdida estocástica de especies en estructuras Gleasonianas o pérdida de especies hiperdispersa en estructuras Uniformes (Dallas and Presley, 2014). Estas últimas seis estructuras cuentan con su cuasi-estructura análoga, definida por el valor de recambio (Presley, Higgins and Willig, 2010).

Cuadro 1. Interpretación de resultados para determinar la estructura de la metacomunidad

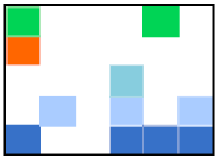
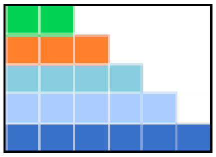
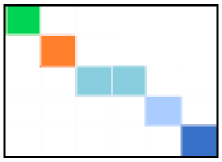
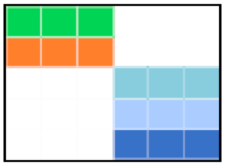
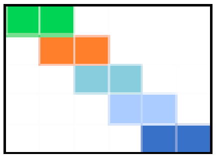
Componente			**Estructura**	
Coherencia	**Recambio**	**Agrupamiento**		
-	/	/	Tablero de Ajedrez	
NS	/	/	Aleatoria	
+	-	-	Anidada	Perdida hiperdispersa de Especies

+	-	NS	Anidada	Perdida aleatoria de especies.
+	-	+	Anidada	Perdida de grupos de especies
+	NS(-)	-	Cuasi-anidada	Perdida hiperdispersa de Especies
+	NS(-)	NS	Cuasi-anidada	Perdida aleatoria de especies.
+	NS(-)	+	Cuasi-anidada	Perdida de grupos de especies
+	NS(+)	-	Cuasi	Uniformemente espaciado
+	NS(+)	NS	Cuasi	Gleasoniana
+	NS(+)	+	Cuasi	Clementsiana
+	+	-	Uniformemente espaciado	
+	+	NS	Gleasoniana	
+	+	+	Clementsiana	

Aplicación de la Teoría de Metacomunidades en Ecología de Enfermedades

El concepto de metacomunidad es poco usado en comunidades de parásitos ofreciéndonos el potencial de explorar los papeles en la historia evolutiva, la limitación en su dispersión, la composición de la comunidad de hospederos y el ambiente abiótico que conduce a la distribución del parásito (Johnson, Roode and Fenton, 2016).

Dentro del contexto de metacomunidades de patógenos se propone que la prevalencia de una infección está influenciada por tres mecanismos: el primero por procesos estocásticos de dispersión, colonización y extinción de patógenos, reservorios y no hospederos, determinando su distribución y potencial interacción. En el segundo mecanismo los cambios antropogénicos pueden filtrar ambientalmente a los hospederos, no hospederos y patógenos. Por último, la diversidad filogenética entre reservorios, vectores y especies no hospederas, puede facilitar o impedir la persistencia y circulación de un patógeno (figura 4) (Suzán *et al.*, 2015). Por lo tanto estos estudios nos permiten entender la ecología de las enfermedades y poder entender, explicar o hasta predecir cambios en las dinámicas de las enfermedades.

Estructura idealizada	Estructura	Definición	Conductor de la infección y prevalencia.	Estructura hipotética
Aleatoria		La distribución de las especies produce patrones aleatorios. Las especies responden diferentemente al mismo gradiente ambiental.	Numero abundante del hospedero reservorio.	
Estructuras no-aleatorias		La distribución de las especies es moderadas por factores de interacciones bióticas y abióticas produciendo subgrupos anidados.		
	Anidada	Rango de especies que ocupan una pequeña porción de el gradiente ambiental dentro de los rangos que ocupan otras especies a lo largo de la porción del gradiente	La prevalencia estará ligada al índice de ocupación del reservorio. Se esperan altas prevalencias si el reservorio tiene una amplia presencia entre los sitios.	
Estructuras anti-anidadas	Tablero de Ajedrez	Pares de especies que son mutuamente excluyentes.	La distribución del reservorio es limitada, baja prevalencia esperada.	
	Clementsiana	Los bordes de los rangos de las especies son altamente coincidentes.	La distribución del reservorio es limitada, baja prevalencia esperada.	
	Gleasoniana	La distribución exhibe un recambio y sus bordes ocurren idiosincráticamente a lo largo del gradiente ambiental.	La distribución del reservorio es limitada, baja prevalencia esperada.	

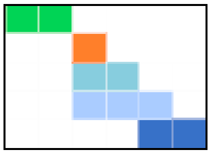
Uniformemente espaciado.	Exhibe recambio y bordes que son hiperdispersos a lo largo del gradiente ambiental, indicando diferencias máximas la tolerancia de las especies.	La distribución del reservorio es limitada, baja prevalencia esperada.	

Figura 4. Estructuras idealizadas de metacomunidades. Modificada de Suzán *et al.*, 2015

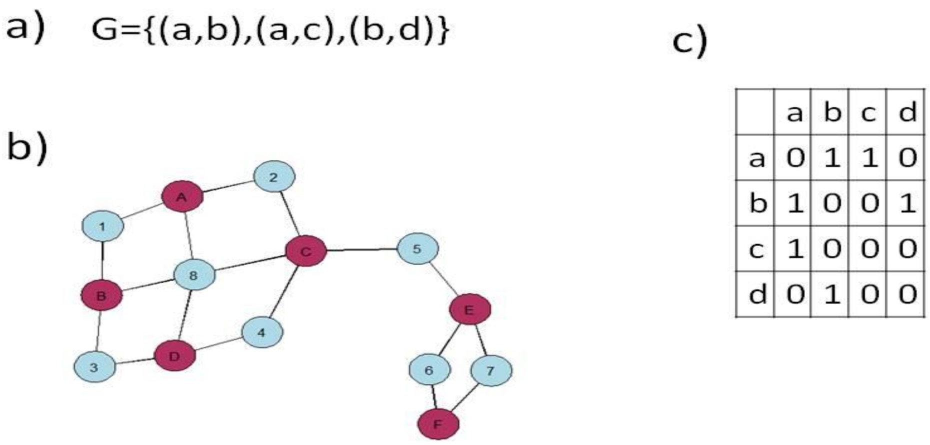
Otras herramientas como la teoría de grafos puede ofrecernos un mejor entendimiento sobre como las interacciones entre las comunidades parásito-hospedero varían espacio-temporalmente. Al utilizarla se corroboran y complementan los resultados que se obtengan de la Teoría de Metacomunidades permitiéndonos ser más puntuales al analizar cada parte de la comunidad tanto de virus como de hospederos, de todo el conjunto y su división natural. Esta teoría se ha ido fortaleciendo en los últimos años, ayudándonos a pronosticar cambios dinámicos en sistemas multipatógeos - multihospederos (Johnson, Roode and Fenton, 2016).

Teoría de Grafos

Las redes se enfocan en las interacciones entre cualquier tipo de entidades para inferir el comportamiento de un gran volumen de datos (Luke and Stamatakis, 2012; Newman, 2014; Hossain and Feng, 2016). Su unión preferente es un proceso natural por lo que captura la noción de elementos en un sistema y sus interconexiones (Hartonen and Annila, 2011; Kolaczyk and Csardi, 2014).

Una red se define de manera más general como una colección de elementos inter-conectados y son un conjunto de puntos (nodos o vértices) unidos por líneas (ligas o aristas), que pueden ser representados en una imagen que describa el modelo (Luke and Stamatakis, 2012; Kolaczyk and Csardi, 2014; Newman, 2014). Las redes pueden ser dirigidas y no dirigidas, dependiendo de si la naturaleza de la relación entre los pares de nodos es unidireccional o bidireccional, respectivamente (Martínez-López, Perez and Sánchez-Vizcaíno, 2009).

Se pueden representar de tres maneras, en notación matemática G ={(ni,nj)}, en un diagrama o grafo, o en una matriz de adyacencia, en la cual se puede representar el numero de contactos entre los nodos (figura 5) (Martínez-López, Perez and Sánchez-Vizcaíno, 2009).



a) G={(a,b),(a,c),(b,d)}

c)

	a	b	c	d
a	0	1	1	0
b	1	0	0	1
c	1	0	0	0
d	0	1	0	0

Figura 5. Tipos de representación de grafos. A) notación matemática, b) diagrama o grafo y c) matriz de adyacencia.

Actualmente se realizan redes con millones de nodos que son imposibles de describir visualmente, por lo que se calculan métricas que nos ofrecen la posibilidad de detectar especies clave en las interacciones parásito-hospedero (Williams, Howe and Hofmockel, 2014).

Para denotar la importancia del nodo se valora la centralidad que es referida con tres medidas, grado nodal, intermediación y cercanía (Martínez-López, Perez and Sánchez-Vizcaíno, 2009; Opsahl, Agneessens and Skvoretz, 2010). El grado nodal se define como el número de contactos que tiene el nodo *i*, entre más alto sea el valor del grado nodal más conectado esta el nodo (Martínez-López, Perez and Sánchez-Vizcaíno, 2009). La intermediación es la probabilidad de que el nodo funja como puente de comunicación a otros nodos que de otra forma no podrían comunicarse (Newman, 2014). La cercanía es la suma de todas las distancias geodésicas del nodo, definiendo la distancia geodésica como el numero de nodos con los que tiene contacto el nodo *i* para poder llegar al nodo *j* (Martínez-López, Perez and Sánchez-Vizcaíno, 2009; Opsahl, Agneessens and Skvoretz, 2010; Newman, 2014).

Otras medidas que nos pueden ayudar en su comprensión son como, el tamaño, que es el número total de nodos y contactos que conforman la red (Martínez-López, Perez and Sánchez-Vizcaíno, 2009). La fragmentación como proporción de pares de nodos que no están conectados con otros. Toma valores de 0 a 1, siendo 1 equivalente a la ausencia de una red por la nula conexión (Martínez-López, Perez and Sánchez-Vizcaíno, 2009). La densidad es la proporción de contactos que pueden existir en la red comparados con los observados. Toma valores de 0 a 1, siendo 0 la ausencia de una red (Martínez-López, Perez and Sánchez-Vizcaíno, 2009) y la asortatividad que nos muestra la fuerte tendencia de asociarse con otros que percibimos como similares a nosotros en algún aspecto, también conocida como homofília (Newman, 2014).

Las redes tienen la propiedad de la estructura de comunidad, es decir, existe una alta probabilidad que cada nodo de un par tengan conexiones a nodos comunes denominado como transitividad (Newman, 2014). Es decir, es altamente probable que dos nodos esten relacionados a otros nodos en común formando una comunidad (Girvan *et al.*, 2002). Por lo tanto, una comunidad es la división de los nodos en grupos de tal manera que las conexiones son más densas dentro de los grupos pero escasas entre los grupos (Figura 6) (Newman, 2016).

Al conocer las comunidades existentes dentro de la red, podemos identificar puentes y puntos de corte; y en caso de enfermedad se puede gestionar el riesgo, previniendo o controlando la propagación de la enfermedad (Martínez-López, Perez and Sánchez-Vizcaíno, 2009). Estos modelos mayormente se aplican para el análisis epidemiológico, teniendo como objetivo identificar patrones de contacto potencialmente-riesgosos entre individuos diseminadores del agente infeccioso presente (Martínez-López, Perez and Sánchez-Vizcaíno, 2009).

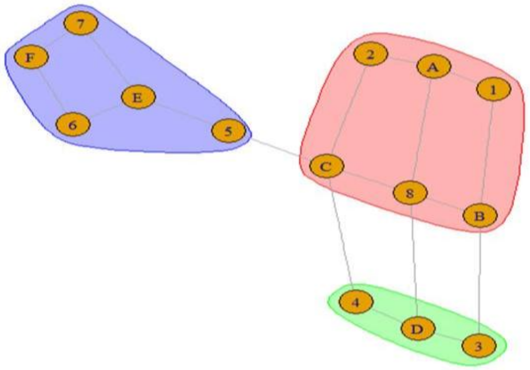


Figura 6. Representación en diagrama de una red con estructura de comunidad. Se pueden distinguir tres comunidades, los miembros de cada una se encuentran sombreados por los colores: rojo, verde y azul.

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Capítulo 2. Viral metacommunities associated to bats and rodents at different spatial scales

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Viral metacommunities associated to bats and rodents at different spatial scales

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Keywords: Biogeographic scale, Disease ecology, Host environmental filtering, Niche theory, Zoogeographic scale.

Abstract: One of the main goals of community ecology is to measure the relative importance of environmental filters to under- stand patterns of species distribution at different temporal and spatial scales. Likewise, the identification of factors that shape symbiont metacommunity structures is important in disease ecology because resulting structures drive disease transmission. We tested the hypothesis that distributions of virus species and viral families from rodents and bats are defined by shared re- sponses to host phylogeny and host functional characteristics, shaping the viral metacommunity structures at four spatial scales (Continental, Biogeographical, Zoogeographical, and Regional). The contribution of host phylogeny and host traits to the meta- community of viruses at each spatial scale was calculated using a redundant analysis of canonical ordering (RDA). For rodents, at American Continental scale the coherence of viral species metacommunity increased while the spatial scale decreased and Quasi-Clementsian structures were observed. This pattern suggests a restricted distribution of viruses through their hosts, while in the Big Mass (Europe, Africa, and Asia), the coherence decreased as spatial scale decreased. Viral species metacommunities associated with bats was dominated by random structures along all spatial scales. We suggest that this random pattern is a result of the presence of viruses with high occupancy range such as rabies (73%) and coronavirus (27%), that disrupt such structures. At viral family scale, viral metacommunities associated with bats showed coherent structures, with the emergence of Quasi- Clementsian and Checkerboard structures. RDA analysis indicates that the assemblage of viral diversity associated with rodents and bats responds to phylogenetic and functional characteristics, which alternate between spatial scales. Several of these varia- tions could be subject to the spatial scale, in spite of this, we could identify patterns at macro ecological scale. The application of metacommunity theory at symbiont scales is particularly useful for large-scale ecological analysis. Understanding the rules of host-virus association can be useful to take better decisions in epidemiological surveillance, control and even predictions of viral distribution and dissemination.

Introduction

The distribution of species can either be explained by random processes, as neutral theory explains (Chave 2004, Hubbell 2005, Gonzalez 2009), or by environmental filters, as Niche Theory proposes (Leibold et al. 2004, Lorencio 2007, Morand and Krasnov 2010 chap. 7).

However, species distributions are influenced by the spatial and temporal contexts in which they occur, thus, neutral theory and niche theory should be tested across a different scale of analysis. There is evidence for the influence of different abiotic factors like temperature and elevation that can determine the organized distribution of species diversity, depending on the spatial scale studied (Rahbek and Graves 2001). The differences in species distributions between scales depend on three factors: physical barriers, the ability to co-occur, and their ability to disperse (Chase and Myers 2011). The diversity of symbionts has not been excluded from this type of analysis (Guernier et al. 2004). A large body of evidence suggest that the distribution of symbionts, defined as all organisms that must infect or inhabit hosts for at least part of their life cycle (Mihaljevic 2012), also responds to environmental filters determined by their hosts (Morand and Krasnov 2010, Mihaljevic 2012, Dallas and Presley 2014). Host phylogeny can act as an environmental filter to symbionts communites due to their interaction in the evolutionary history, co-adaptation and ecosystem process in the community (Streicker et al. 2010, Krasnov et al. 2014, Córdova-Tapia and Zambrano 2015). Similarly, the host functional characteristics can play a role as an environmental filter due to shared life histories or by spillover events (Davies and Pedersen 2008, Morand and Krasnov 2010).

We used viral communities associated with rodents and bats to analyse the effect of environmental filters. Rodents and bats are the most diverse orders of mammals thus they constitute suitable model taxa to explore the viral diversity providing relevant information to understand the dynamics of virus-host distribution (Lorencio 2007). These taxa have been recognized as the main reservoirs of a high number of zoonotic viruses, some of them with an enormous impact in public and animal health (Luis et al. 2013, 2015). Besides the individual approach, the study of the association between host and virus requires a clear understanding of the ecological context of infection and transmission be required (Woolhouse 2001, Suzán et al. 2015, Johnson et al. 2016). Because the host-virus system is intimately embedded within the communities, it is possible to recognize the existence of an organization in the distribution of viral diversity and later recognize the filters that allow or not to associate with a host (Suzán et al. 2015). The dispersion of a virus within a host community is accomplished through transmission events and may depend on the viral richness present in the community, so it is common to have multi-pathogen systems that can be considered as metacommunity (Suzán et al. 2015). Metacommunity theory implemented in viral communities at different spatial scales in combination with a redundancy analysis allows identifying the factors that facilitate virus distribution among hosts (Mihaljevic 2012, Dallas and Presley 2014, Suzán et al. 2015). Based on the metacommunity structures proposed by Leibold and Mikkelson (2002), and mechanisms for infection and prevalence proposed by Suzan et al. (2015), we can expect Random, Checkerboard and Clemenstian viral structures. A widespread distribution of abundant reservoir species are related with random structures while a limited viral distribution or a high viral specificity are related with Checkerboard or Clementsian structures (Suzán et al. 2015). The factors that shape viral communities and their distribution through their host at different spatial scales have not been studied. To measure the influence of the host phylogeny and functional characteristics of the host on viral community structure we hypothesized that both the expression of Clementsian structures based on the Niche Theory would prevail at different macroecological scales, and the host phylogeny will explain the viral metacommunity distribution as response of the shared host evolutionary histories and ecological relationships. We analyzed the contribution of phylogenetic and functional factors to the structure of viral metacommunities associated with rodents and bats. In our model, the viral community is defined as all viruses detected in each host species inside the geographic scale to analyze. In this analysis, the metacommunities are composed by viral communities linked by processes of dispersion and transmission between hosts.

To consider the spatial scale, the first analysis of viral metacommunities was performed on a Continental scale considering the ocean as the main geographic barrier for viral distribution. The subsequent macroecological scales were selected by their similarity on diversity composition as Biogeographical scales, recognized by their similarity in plant diversity (Cox 2001). Zoogeographical scales by their similarity in animal diversity (Holt et al. 2013), and Regional scales that contain local shared evolutionary histories (Holt et al. 2013).

Methods

We constructed a database based on reports of viruses isolated or detected by molecular techniques in bats and rodents. We recorded the host species, the virus species, and viral family according to the International Committee of the Taxonomy of Viruses (ICTV) (https://talk.ictvonline.org/). The bat viruses information was collected from DbatVir database (http://www.mgc.ac.cn/DBatVir/), and data from rodents were collected by a literature search in Web of Science (https://webofknowledge.com), Elsevier (https://www.elsevier.com/advanced-search) and World Wide Science (https://worldwidescience.org/) with the keywords: "rodent", "virus", "PCR" and "wild". The registered information was collected from years 1956 to 2015 and only studies with molecular techniques were considered. The geographic location was registered and classified into four spatial scales (Fig. 1): 1) According to the continental scale: America, Oceania and "Big Mass" that includes Europe, Africa, and Asia. 2) Biogeographical scale: Nearctic, Neotropical, Palearctic,

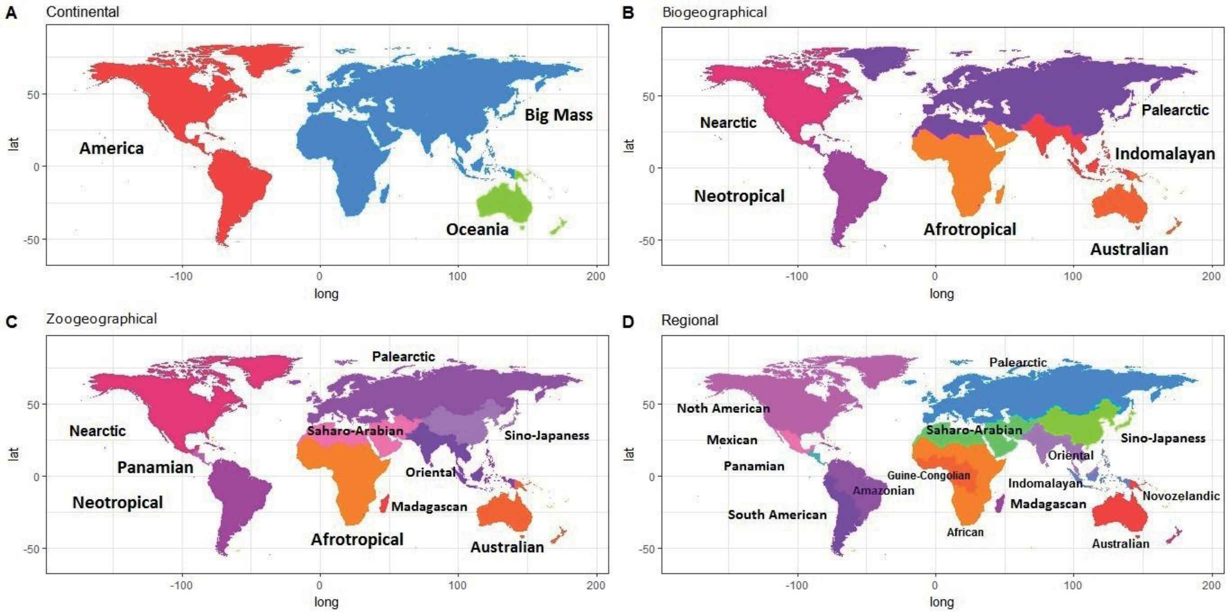

Figure 1. The framework of the spatial scales analyzed.

Afrotropical, Indomalayan and Australian (Cox 2001) 3) Zoogeographical scale: Nearctic, Panamian, Neotropical, Palearctic, Afrotropical, Oriental, Saharo-Arabian, Sino-Japaness, Madagascan and Australian (Holt et al. 2013).
4) Regional scales: North American, Mexican, Panamian, South American, Amazonian, Palearctic, African, Guine-Congolian, Madagascan, Indomalayan, Oriental, Saharo-Arabian, Sino-Japaness, Novozelandic, and Australian (Holt et al. 2013).

Detection of metacommunity structures

A presence-absence data matrix was constructed for each spatial scale and for each viral taxonomic level (species and family), where the virus was the column and the host the row. We obtained 62 rodent and 68 bat matrices, but due to the measures and the capacity of the algorithm performed in the metacommunity structure analysis, we could only obtain results of 24 and 38 matrices respectively. To evaluate the metacommunity structure of virus-host species form each matrix, we measure three properties. The coherence as the degree to which pattern can be collapsed into a single dimension, turnover counting the number of species replacements along the matrix and boundary cumpling measuring how the edges of species boundaries are distributed along this dimension (Leibold and Mikkelson 2002). The analysis of metacommunity structure was performed with the metacom package (Dallas 2014) implemented in R (R Core Team 2017), and the detection of metacommunity structure was using the Presley's decisions tree (Presley et al. 2010).

Covariation of host characteristics with the viral metacommunity structure

We measured the influence of the host phylogeny and functional characteristics of the host on viral community structure. The phylogenetic component was estimated taking the two first components of the **PCoA analysis on the phylogenetic distance matrix, which w**as obtained by extracting the host species from the mammalian super-tree hosts (Bininda-Emonds et al. 2007) with the "picante" package. We include the body mass, litter size, number of litters per year and trophic guild, as host functional characteristics that may explain variation among hosts in viral community composition and their influence on the viral transmission. The variables were obtained from PanTHERIA database (Jones et al. 2009), Animal Diversity Web (http://animaldiversity.org) and Encyclopedia of Life (http://eol.org/). A redundant analysis of canonical ordination (RDA) has been performed to detect the relationship between the host phylogenetic component and host functional characteristics in the metacommunities from each spatial scale to obtain the explaining percentage on each one of detected metacommunity structures. The RDA was calculated with the algorithm varpart (Peres-Neto et al. 2006) of "vegan" package (Oksanen et al. 2016) implemented in R. This function performs a partition of the variation in community data for the explanatory variables.

Results

Database

The rodents' database has 825 records, and includes 172 rodent host species, 124 virus species distributed in 23 viral families, of which 70 species and 14 families are zoonotic. The bats' database has 4,659 records and includes 220 host bats species, 174 virus species and 29 viral families of which 41 virus species and nine viral families are zoonotic.

Metacommunity structures

Rodents. We detected a Quasi-Clementsian structure in the metacommunities of viruses in the American Continent, and the distribution of these virus species was partly explained by host phylogeny (29%). The Big Mass scale showed a Clementsian structure explained by a low percentage of host functional characteristics (0.2%) (Table 1). Oceania continent was not included in the analysis because only four records were obtained. At Biogeographical level, a Clemenstian structure was detected in the Nearctic region, a Quasi-Clementsian structure in the Neotropic and Palearctic, and a random structure was found in the Afrotropical Region.

At Zoogeographical scale, only four regions were analyzed including Afrotropical with Quasi-Clemenstian structure, Nearctic with Clementsian and Palearctic and Oriental with Random structures. At Regional scale, three regions were analyzed including North Amercian, with Clementsian structure, African and Palearctic with Random structures. No relevant results were observed at metacommunities of viral families, where the random structures dominated in all scales except for Nearctic Biogeographic and Zoogeographic scale where a Quasi-Clementsian structure was detected.

Chiropterans. Except for the Big Mass scale where a Quasi-Clementsian structure was detected, the rest of the 19 viral species metacommunities analyzed showed Random structures. Oceania continent with 11 records was not possible to analyze. At biogeographic and zogeographical scale, Afrotropical and Palearctic regions presented a Quasi-Clemenstian structure, while we detected a Checkerboard structure in the Neotropical zoogeographical region. Only the Quasi-Clementsian structure of the Palearctic zone is maintained up to the Regional scale. At all scales, the host phylogeny and host functional characteristic explain the distribution of the viral families (Table 2).

Discussion

Rodents

We observed different patterns at different scales of analysis. For example, in the American Continent the coherence increases as the geographic scale decreases, as shown in regional scales. Contrarily, in the Big Mass an opposite pattern was found; the coherence decrease with a decreasing geographic scale (Fig. 2). In the American continent these patterns may

Table 1. Results of the analysis of coherence, range turnover, and boundary clumping for the viral metacommunities of rodents and results of RDA analysis. Abs, embedded absences; SD, standard deviation; df, degrees of freedom. Q-Clem.=Quasi-Clementsian.

Spatial Scale / Community	Coherence				Turnover				Boundary clumping			Metacommunity	RDA Analysis	
	Abs	p	Mean	SD	Rep	p	Mean	SD	Index	p	df	Structure	varpart	%
Continental														
America	9	0.05	49.24	20.88								Random	phylo/ phylo+fun	29 / 0.14
Big Mass	66	0.01	163.60	36.18	5884	0.03	10031.24	1874.44	2.18	0.00	41	Clementsian	fun	0.26
Biogeographical														
Nearctic	17	0.01	68.61	20.94	1865	0.01	3656.22	711.63	3.41	0.00	39	Clementsian	phylo/fun	10 / 6.6
Neotropic	3	0.04	29.74	13.19	1329	0.13	1906.22	377.90	2.63	0.00	24	Q-Clem.	phylo+fun	0.9
Afrotropical	23	0.05	52.23	14.99								Random	0	
Palearctic	96	0.00	256.43	36.10	6303	0.05	10560.87	2192.90	2.28	0.00	31	Q-Clem.	phylo+fun	0.9
Zoogeographical														
Palearctic	136	0.36	156.01	21.69								Random		
Afrotropical	23	0.04	51.32	13.82	1242	0.46	1461.81	298.22	2.91	0.00	21	Q-Clem.	phylo+fun	1.6
Regional													0	
North America	17	0.01	66.50	19.94	1671	0.03	3192.51	684.30	3.72	0.00	37	Clementsian	phylo/fun	10.8 / 6.7
African	15	0.13	29.29	9.44								Random	phylo+fun	19

Table 2. Results of the analysis of coherence, range turnover, and boundary clumping for the viral metacommunities of chiropters and results of RDA analysis. Abs, embedded absences; SD, standard deviation; df, degrees of freedom. Q-Clem.=Quasi-Clementsian.

Spatial Scale / Community	Coherence				Turnover				Boundary clumping			Metacommunity	RDA Analysis	
	Abs	P	Mean	SD	Rep	P	Mean	SD	Index	P	df	Structure	varpart	%
Continental														
America	177	0.2187	130.817	37.5543								Random	fun	0.8
Big Mass	782	0.32	866.77	85.77								Random	phylo+fun	1.78
Biogeographical														
Nearctic	32	0.55	41.88	16.39								Random	phylo+fun	2.41
Neotropic	97	0.67	106.90	23.48								Random	phylo+fun	1.7
Afrotropical	109	0.03	192.29	38.23	1606	0.14	4838.85	2167.68	7.77	0.00	14	Q-Clem.	phylo+fun	6.28
Palearctic	649	0.02	815.98	70.05	8618	0.05	27181.60	9668.56	8.15	0.00	23	Q-Clem.	0	
Indomalayan	28	0.23	37.93	8.29								Random	phylo+fun	11.42
Zoogeographical														
Nearctic	32	0.38	47.31	17.34								Random	phylo+fun	2.02
Neotropic	111	0.00	52.91	18.90	413	0.13	1066.47	436.64	2.15	0.00	7	Checkerboard	phylo+fun	1.28
Palearctic	167	0.03	225.11	26.72	2150	0.19	3954.92	1368.93	3.95	0.00	17	Q-Clem.	phylo+fun	0.83
Afrotropical	88	0.02	153.69	27.66	768	0.09	3195.48	1421.86	7.03	0.00	14	Q-Clem.	phylo+fun	8.01
Oriental	28	0.25	37.81	8.48								Random	phylo+fun	11.42
Sino-Japanese	322	0.20	368.74	36.43								Random	phylo / fun	7.5 / 6.09
Regional														
South America	12	0.25	27.11	13.20								Random	phylo+fun	2.46
African	31	0.27	44.46	12.26								Random	phylo+fun	1.79
Guineo-Congolian	27	0.06	48.07	11.22								Random	phylo/fun	4.19/2.22
Oriental	11	0.48	14.03	4.33								Random	phylo+fun	28.76

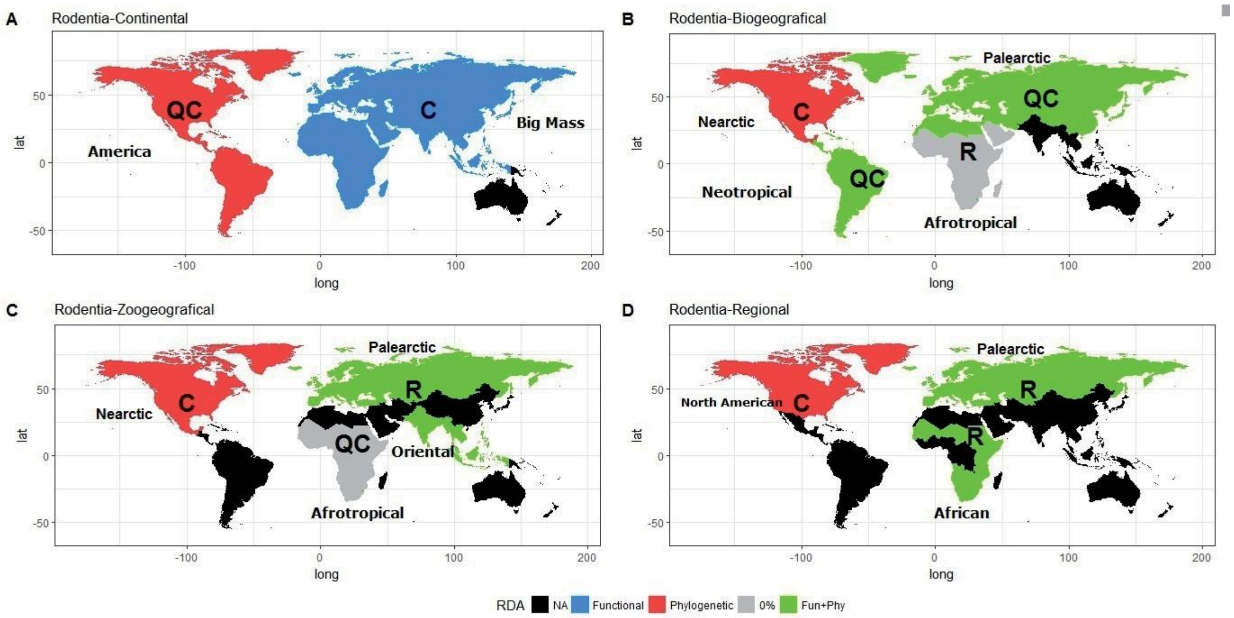

Figure 2. Structures of viral species metacommunities detected in rodents. Letters refer to the metacommunity structure: QC, Quasi-Clementsian; C, Clementsian, R, Random. The colors represent the variable that explains the viral distribution within the metacommunities obtained by the RDA analysis: Black, regions without enough data to detect a structure; Blue, functional characteristics; Red, host phylogeny; Gray, the RDA analysis resulted in zero and Green, combining host phylogeny and functional characteristics.

be explaining by the high influence of the latitudinal gradient on the host distribution and by the island biogeography and the edge effect because the American Continent has a higher border surface (Lovejoy et al. 1986). Instead, the Big Mass surface allows a homogeneous host distribution (Buckley et al. 2010). At the Big Mass scale there are not strict physical barriers between bioregions and viruses are widely shared at the edges, mainly at the Palearctic-Afrotropical edge. These boundaries merged many years ago, forming a large area that allowed this exchange of viral diversity, so they are now arbitrary limits (Morand and Krasnov 2010). Therefore, it was possible to detect a Clementsian structure in the Big Mass metacommunity, but when the spatial scale decreased we observed a dominance of Random structures. At smaller communities, the characteristics of the host species are more widely shared without delimiting niches, and therefore the viral distribution depends on its capacity of dispersion rather than local filters.

In the Nearctic Biogeographic region, the Clementsian structure was explained by host phylogeny in 10% (Table 1), suggesting a phylogenetic signal and therefore, a higher specificity for host clades. The Quasi-Clementsian structure detected in the Neotropical Biogeographical region showed a weak response to environmental host filters (0.9%). When we compare these two regions, they show a response to a latitudinal diversity gradient (Kaufman 1995, Gaston 2000, Guernier et al. 2004), suggesting a greater diversity of host and viruses in the tropics probably influenced by a constant temperature (Morand and Krasnov 2010). This property facilitates the survival and viral mutations, facilitated by vectors proliferation, incrementing the chance of spillover, giving rise to generalist symbionts (Harvell et al. 2002).

The coherence in the structure of the Afrotropical zoogeographical region increases by the loss of the Middle East region, which was included at biogeographical scale and prevented the potential viral dispersion. Functional and phylogenetic characteristics explained the random structure detected in the African Region by 19% (Table 1). This percentage can be explained by the absence of *Thryonomys swinderianus* and *Xerus erythropus*, species in the African region who contained extreme values in their phylogenetic characteristics. It also shows a structure with a Clementsian tendency that is disturbed by *Mastomys natalensis*, a rodent associated with seven of the 14 viruses in this scale, in comparison with the remaining 21 rodents that host 1-4 virus species. Also, it is the only species in this level with reports of Banzi virus, Gairo virus, Mopeia and Morongo virus. Probably because of its anthropism and the most considerable sampling effort.

In Rodents we can assume that coherence decrease in viral families metacommunities may emerge due to the loss of information of viral species characteristics when viral families data was analyzed.

Chiropterans

The metacommunity structure of viral species associated with bats was dominated by a Random structure, however, the distribution of the viruses is not aleatory because most of the metacommunities were explained by the host phylogeny and functional characteristics. Besides some viruses associated with Chiropterans are cosmopolitan, like Rabies virus, which have a wide range distribution within the metacommunitiy preventing the detection of a coherent structure.

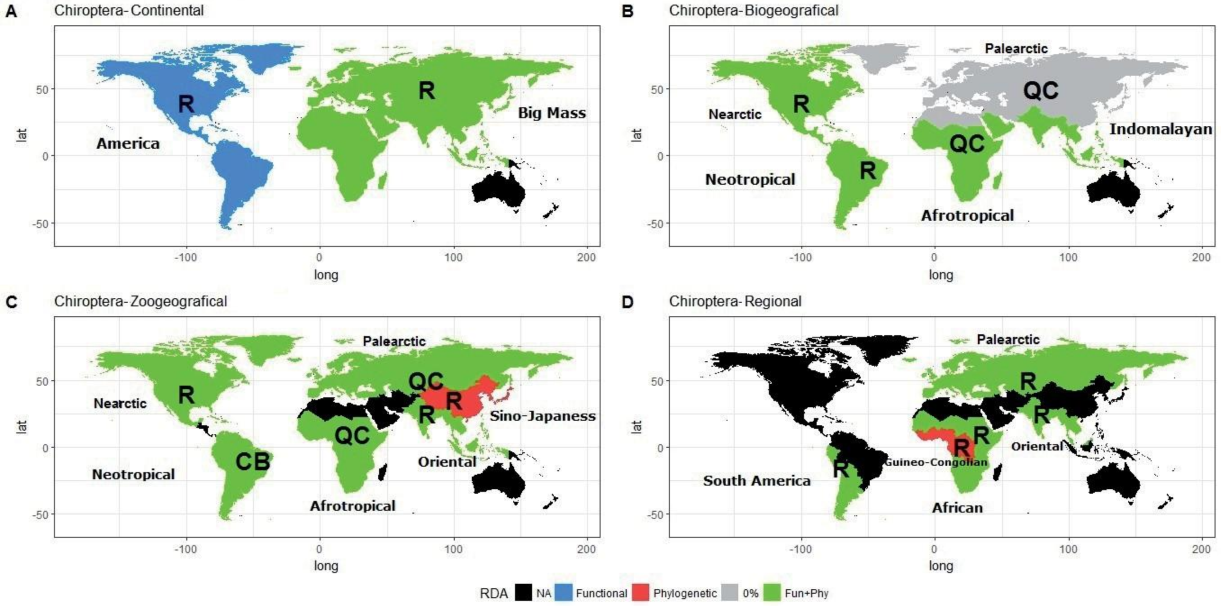

Figure 3. Structures of viral families metacommunities detected in chiropterans. Letters refer to the structure: QC, Quasi-Clementsian; C, Clementsian, R, Random, CB, Checkerboard. The colors represent the variable that explains the viral distribution within the metacommunities obtained by the RDA analysis: Black, regions without enough data to detect a structure; Blue, functional characteristics; Red, host phylogeny; Gray, the RDA analysis resulted in zero and Green, combining host phylogeny and functional characteristics.

In chiropterans, contrary to rodents, higher coherence at viral family scale suggests a clustering pattern of viral families. Besides, their classification of viral species is more specific, they even take the name of the host in which they were isolated.

The coherence of viral families metacommunities was only detectable at Biogeographical and Zoogeographical scales, while in the Continental and Regional scales the coherence cannot be observed. This result can be explained by removal of the host and viral families with a wide range of distribution, due that our model assumes a homogeneous distribution of host and viruses.

At America Continent scale, we detected several Random and Checkerboard structures in viral families metacommunities due to the presence of cosmopolitan viruses with a high sampling effort due to their public health relevance, such as the Rhabdoviridae and Coronaviridae families, found in 73% and 27% of the host species distributed in America respectively.

In the Palearctic and Afrotropical Biogeographic regions a Quasi-Clementsian structure was detected. When analyzing the Palearctic region at Zoogeographical scale, we can observe a coherence increase due to a separation of random structures which belong to the Zoogeographical regions Saharo-Arabica and Sino-Japanese (Fig. 3), with a low sampling effort. Despite this, the Sino-Japanese region is explained by phylogenetic (5.32%) and functional (6.09%) characteristics but separately, because the region contains extreme climates (Urteaga 1993) that could generate divergence of host and viruses (Gorman et al. 1992).

The random structure observed in Oriental Regional scale was explained by a high value (28.7%) of environmental host filter (phylogeny + functional characteristics). This result suggests that the absence of a coherent structure is resulted by the poor sampling effort in the area.

The virus families' distribution in the Quasi-Clementsian structure detected in the Afrotropical Biogeographic region is explained by environmental host filters (6.2%), however, when the geographic scale decreases the coherence increases with environmental host filter (8.2%). This increase of coherence can be explained by the absence of Madagascan region due to the geographic barrier that prohibits host migration. Meanwhile, the host migration between African and Guineo-Congolian Regions could be possible, explaining the decreases of coherence and the random structures detected in these two regions.

General patterns

In general, a higher number of Clementsian and Quasi-Clementsian structures was observed in response to environmental host filters. The viral distribution responds primarily to dispersion filter by the geographic scale and secondly to the host characteristics, being affected by two types of simultaneous filters, at different spatial scales.

Random structures are explained by taking into account the information biases and the dynamism in which the ecosystems are involved, undergoing constant changes, of which we only manage to capture moments of their history. In spite of random spatial structures, host-virus relationships can still be highly specific, suggesting coevolution between hosts and viruses (Drexler et al. 2010) including coronaviruses (CoV, however our framework addressed to community scale can not measure these events. Even so, the rules of community assembly are not a law, and they are only one of several mechanisms that alternate, so it proposes the predominance of Clements superorganism at macroecological level (Jaisson 2000). Thus, the study of such viral community assembly rules must be deepened to understand these processes.

Clarifying the influence of these environmental host filters, enables us to address the effect of differential study efforts and also to plan surveillance systems and responds to situations like emergent diseases. To understand and predict viral transmission dynamics it is important to identify those variables that explain viral distribution through their hosts. If the viral distribution is explained by the phylogenetic component we will be able to predict new hosts based on the phylogenetic similarity. Instead, if viral distribution is explained by the functional component we could predict new hosts based on functional traits similarity. We must not forget that multiple factors interact and affect the direction of changes in viral metacommunities so that their dynamism must be monitored and understood by multidisciplinary approaches.

Conclusion

In general, it is more feasible to analyze the viral metacommunities associated with rodents at viral species scale by overlapping families, showing a weak phylogenetic signal between the host and the virus species. Bats, on the other hand, showed more order at the viral family level due to viral taxonomic classification, but also present more cosmopolitan viruses.

These inferences were based on the currently available data. Unfortunately, the present data set is insufficient to analyze the virus assemblages of small regions like the Australian and Madagascan due to the scarcity of data. Our data set is also likely to be biased because synanthropic species and viruses of public health relevance were sampled heavily, and this likely interferes with the influence of natural structures.

However, at the macroecological level, viral metacommunities associated with Rodentia and Chiropterans showed Clementsian structures or at least tended to them (quasi-Clementsians). The viral metacommunities mainly respond to spatial abiotic constraints, and secondarily to host environmental filters, which offer us an approach for the understanding of these clusters that explain a part of the set.

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Appendix

Supplementary Table 1. Results of the analysis of coherence, range turnover, and boundary clumping for the viral families metacommunities of rodents and results of RDA analysis. Abs, embedded absences; SD, standard deviation; df, degree freedom.

Supplementary Table 2. Results of the analysis of coherence, range turnover, and boundary clumping for the viral species metacommunities of bats and results of RDA analysis. Abs, embedded absences; SD, standard deviation; df, degree freedom.

The file may be dowloaded from www.akademiai.com.

Capítulo 3. Viral networks and detection of potential zoonotic viruses in bats and rodents: a worldwide analysis

Viral networks and detection of potential zoonotic viruses in bats and rodents: a worldwide analysis

ABSTRACT

Bats and rodents are recognized to host a great diversity of viruses and several important viral zoonoses, but how these viral diversity is structured, how viruses are connected, shared and distributed among host networks is barely understood. To understand this, we compared the associative capacity of the host-virus networks in rodents and bats with the identification of those viruses with a zoonotic potential. A virus database, detected by molecular methods, was constructed in the two taxonomic groups. We registered 5,484 records, 825 in rodents and 4,659 in bats. We identified a total of 173 and 166 viruses in rodents and bats of which 53 and 40 are zoonotic viruses, respectively. Based on a network theory, a non-directed bipartite host-virus network was built by each group. Subsequently, the networks were collapsed to represent the connections among hosts and viruses. We identified both discrete and connected communities. We observed a greater degree of connectivity in bat viruses and discrete communities in rodents. The coronaviruses registered in bats, have the highest values of degree, betweenness and closeness centralities. In rodents, higher degree positions were distributed homogeneously between viruses and hosts. At least in our database, a greater proportion of rodent zoonotic viruses were detected. Then rodents should not be underestimated as important reservoirs of zoonotic disease. We found that viruses were more frequently shared among bats than in rodents. Using the network theory macroecological ptterns may bie identified and some risk may be revealed, for instance we identified that parvovirus in megabats and Gbagroube virus in rodents may represent a zoonotic risk due to the proximity to humans and other zoonotic viruses. Other taxonomic groups such as primates and birds should be analyzed with multi-host and multi-pathogen frameworks to understand host-virus assemblages and their implication to the public health.

Keywords: (3-6) disease ecology, viral diversity, host-parasite network, zoonoses

INTRODUCTION

Bats and rodents are hosts of a significantly proportion of zoonoses, even higher than all present in other mammalian orders. Over 200 viruses belonging to 27 viral families have been isolated or detected in bats, however, bat-human transmission has only been observed on eleven viruses belonging to four different viral families: Rhabdoviridae, Filoviridae, Coronaviridae, and Paramyxoviridea (Allocati et al., 2016). Some viral examples are: coronaviruses, Sosuga virus, Ebola virus and Marburg virus, rabies and rabies-related lyssaviruses, Nipah and Hendra viruses and paramyxoviruses, including rubulaviruses (Allocati et al., 2016; Calisher, Childs, Field, Holmes, & Schountz, 2006; Hayman, 2016; O'Shea et al., 2014; Plowright et al., 2015).

Similar to bats, as we have been mentioned, Rodents have similar zoonotic potential. They are associated to a large number of zoonotic viruses. Examples of viruses associated to rodents are Hantavirus, Sin nombre virus, Puumala virus, Crimea-Congo hemorrhagic fever virus, Kyasanur forest virus, tick-borne encephalitis virus, Lassa fever virus, Venezuelan equine encephalitis virus, and other virus. All of the mentioned viruses associated to bats and rodents, have a great impact on public health. However, we need to take in a count that not all the viruses are pathogens; some of them have co-adaptation with their host.

Previous studies had explored the viral associations on a more restricted scale. For example, Hayman et al. (2016) propose maps of viral distributions by the distribution of hosts families. In contrast, with a phylogenetic approximation, Streicker et al. (2010) explored rabies associations and Cui et al. (2015) compared only retrovirus associations between bats and rodents. Also Anthony et al. (2017) explored coronaviruses networks at host family level. Finally, Borges et al. (2016) analyze the relations of the zoonotic diseases in South-East Asia, it´s to say, not in a global level.

Han et al. (2016) situate bats and rodents in the same category with high zoonotic potential, but other researches examine the difference between bats and rodents. Different hypotheses and theories have been proposed to examine and comprehend the characteristics that support bats with such capability (Brook & Dobson, 2015; Moratelli & Calisher, 2015) Today, the viral diversity we know and connectivity through the diverse species of bats have been fairly understood (Moratelli & Calisher, 2015; O'Shea et al., 2014) and the implications for emerging and reemerging zoonoses are barley known.

The literature explaining why bats harbor several viruses is extensive but do not describe the virus associations at: (1) the host level (species), (2) the direct partnership, (3) the whole species of viruses, (4) the statistics of associations and neither (5) the metrics that characterize the associations.

Bats and rodents are similar because rodents are a highly diverse and ancestral mammals with similar life histories to bats (Luis et al., 2013). They have been recognized as reservoirs for various zoonotic viruses (Han, Schmidt, Bowden, & Drake, 2015). For instances, hantaviruses (Schmaljohn & Hjelle, 1997) and arenaviruses (Charrel & de Lamballerie, 2010). But we recognize differences in their viral associations that change the zoonotic potential of wich one. In disease ecology, relevant analytical tools have been exploited to holistically explain the dynamics of infections and providing novel hypothesis explaining macroecological patterns (Johnson, Roode, & Fenton, 2016).

One of the theories that helps to predict dynamic changes in host-pathogen systems is the graph theory (Bordes, Caron, Blasdell, de Garine-Wichatitsky, & Morand, 2017; Johnson et al., 2016). This approach provides us a better understanding on how interactions take place within pathogen communities, how hosts are connected with pathogens, their preferred association, and their transmission patterns (Godfrey, 2013; White, Forester, & Craft, 2017).

The graphs, better known as networks, focus on the interactions between any type of entities (Newman, 2014), and they have the potential to infer relationships within a larger framework (Hossain & Feng, 2016; Luke & Stamatakis, 2012). A network is capable of emphasizing the preferred union as a process (Hartonen & Annila, 2011). Then, it captures the notion of elements in a system as well as relevant interconnections (Kolaczyk & Csardi, 2014). This kind of analysis could be used to: describe viral diversity associated to different hosts, detect hosts and viruses that share associations, and therefore make up a group that is distinguished by similar characteristics (White et al., 2017).

In the network theory, centrality and dispersion metrics are calculated to recognize the importance of each member component (Martínez-López, Perez, & Sánchez-Vizcaíno, 2009; Newman, 2014; Opsahl, Agneessens, & Skvoretz, 2010). In terms of disease ecology, we can employ the idea to explore the host-host, virus-host, and virus-virus interactions by the networks collapse and by communities' detection. Therefore, the network analysis offers the opportunity to recognize viruses and hosts with great diversity due to their high degree and bats and rodents are excellent examples. They are "pools" with highly adaptable viruses and hosts with high resistance. With the betweenness measure, we can recognize dispersing hosts and key viruses in the evolution or viral transmission (Opsahl et al., 2010; White et al., 2017). The closeness measure makes out hosts and viruses that may have little connectivity but are surrounded by important nodes highly connected (Opsahl et al., 2010; White et al., 2017).

Therefore, the present study aimed to compare and recognize the differences in the associative capacity of the host-virus networks in rodents and bats as well as to identify the viruses that may shift across species including humans suggesting a zoonotic potential.

METHODS

Database

In this study different sources of data were scrutinized. More specifically, in bats, we retrieved data from a single database called DbatVir (http://www.mgc.ac.cn/DBatVir/) whereas we gathered data on viruses in rodents from Web of Science (https://login.webofknowledge.com), Elsevier (https://www.elsevier.com/advanced-search) and World Wide Science (https://worldwidescience.org/).

In those databases we used the next keywords: rodent, virus, PCR, wild and zoonotic. Then, we constructed two separated large databases of viruses isolated from rodents and bats. Moreover, when the taxonomic classification was not clear, we searched in the ICTV (https://talk.ictvonline.org/) to classify the viruses. Subsequently, according to the literature, the viruses were classified into direct zoonotic and non-zoonotic pathogens (Allocati et al., 2016; Calisher et al., 2006; Han et al., 2015). To analyze the certain viral associations, viruses only detected by molecular methods were included in our study.

Overall Networks Analyzes

Two independent undirected bipartite networks were built for the orders of Rodentia and Chiroptera. It is to say, the networks were constructed with two types of nodes: virus and host. The connections in the network defined the detection of the virus over the host, and a node denoted a specific species in these orders. Also, we add a human node connected when the virus was classified as zoonotic. This helps us to group and identify zoonotic viruses and viruses close to him, facilitating identify viruses with zoonotic potential. Then, host-to-host and virus-to-virus networks were constructed with the purpose to explore these networks in different dimensions. The “bipartite.projection” function in the igraph package implemented in R software version 3.4.2 (R Core Team, 2017) was employed to collapse the bipartite network. Basically, a host was connected to another host when they share a common virus (Figure 1).

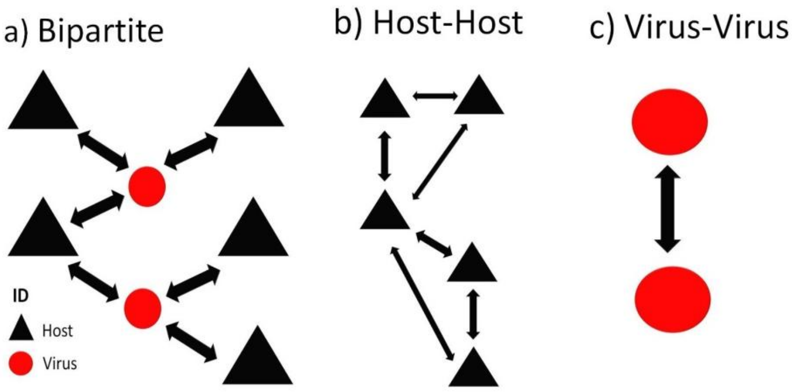

Figure 1. Collapsed Networks: a) Bipartite network, b) Collapsed host-host network and c) Collapsed virus-virus network.

Collapsed networks

In the collapsed network, the host nodes were conserved, and the virus nodes were transformed into the weight of corresponding links in order to illustrate the relationships among different hosts (Figure 1a and 1b). Likewise, the virus-virus relationship was highlighted by collapsing the host nodes into the weighted links. Two virus-virus networks were produced; one for rodents and another for bat species (Figure 1c).

Network measurements

We measured the networks in two levels: individual node and the entire network. At the node level, we measured different centrality values including: degree (number of links that a node has), betweenness (number of times a node is an intermediary to connect each possible pair of nodes) and closeness (the degrees of average separation in relation to other nodes) (Martínez-López et al., 2009; Newman, 2014). At the network level, we measured density and diameter. More specifically, network density is the proportion of contacts that are actually observed in the network divided by those that could possibly occur. As well as, diameter is the length of the longest geodesic distance (Newman, 2014).

We use these measurements to demonstrate the big picture of the network and identify the key nodes that closely related to humans. To calculate the measures of the networks we used algorithms provided in the packages ‘igraph’ (Csárdi & Nepusz, 2006) and ‘network’ (Butts, 2008) in program R (Table 1). Next, the relevant plots were produced using functions in the packages ‘igraph’ and ‘ggplot2’ (Gómez-Rubio, 2017) implemented in software R (R Development Core Team, 2011).

Table 1. Formulas applied to calculate network parameters.

Measure	Formula	Reference
Degree centrality (D)	$D = \sum_{i=1}^{n} a(p_i, p_k)$	(Freeman, 1978)
Betweenness centrality (B)	$B = \sum_{i}^{n} \sum_{< j}^{n} \frac{g_{ij}(p_k)}{g_{ij}}$	(Freeman, 1978)
Closeness centrality (C)	$C = \frac{n-1}{\sum_{i=1}^{n} n_d(p_i, p_k)}$	(Freeman, 1978)
Density (ρ)	$\rho \frac{2E}{n(n-1)}$	(Martínez-López et al., 2009)
Diameter (Ø)	$max_{ik}\ d(i,k)$	(West, 2005)

Parameters explained: $n,$ number of nodes; p_i, node of origin; p_k, node of destination; g_{ij} number of geodesic linkages; n_d, number of edges in the geodesic linkage; E, number of edges and d, graph distance.

Community detection

Communities were detected with Maximization of Modularity method (Newman, 2016) using the function "cluster_edge_betweenness" (Girvan, Girvan, Newman, & Newman, 2002; Newman & Girvan, 2003) equipped in the 'igraph package' (Csárdi and Nepusz 2006). That is, the algorithms recognize nodes with dense and weak connections between groups. With this method, the nodes with dense connections with humans were identified.

$$Q(\gamma) = \frac{1}{2m} \sum_{ij} (A_{ij} - \gamma \frac{k_i k_j}{2m}) \delta_{g_i g_j} \qquad (1)$$

Where m denotes the total number of links in the network, A_{ij} refers to the actual number of links between nodes $_i$ and node $_{j,}$ γ is a parameter calculated by the algorithm; K, degree of i; $\delta_{g_i g_j}$ is a randomized number of links between a pair of nodes. The communities' detection helps to recognize groups of hosts that share viruses and viruses that share hosts, therefore they may continue to exchange with each other since they have similar characteristics among them.

Subnetwork

A subnetwork was built by choosing communities with more than 4 pair of members, which is over the minimum number accepted in statistical normality samples (n=3) (Royston, 1982; Statistics, Hammer, Harper, & Ryan, 2008). These subgraphs were illustrated to gain better community visualization and being able to recognize the most relevant communities for the detection of potentially zoonotic viruses.

Subcommunities

From the subnetwork, the most important communities were chosen according to the measures of the members (top-five nodes) in the first instance and the number of zoonotic viruses (80%) as selection criteria. After that, a sociogram representing the preferential unions and the complex interaction on the biggest communities was constructed using the package ‘visNetwork’ (Almende & Thieurmel, 2016) in program R. This choice helps us to focus and observe in more detail the interactions within these important communities.

RESULTS

Database

The database of rodents contains 825 records including 172 rodent species and 123 viruses, of which 53 are zoonotic viruses. In the bat database, 4,659 records were retrieved. That is, 220 bats species associated with 166 viruses of which 40 viruses were classified as zoonotic. Both databases are detailed in Appendix 1.

Rodentia Network

Overall Network Analyzes

In total, 269 nodes were found with 323 links (Figure 2.A). In relation to the diameter, the Rodentia network was nine and the density was 0.0044. Also, we found that *Mus musculus* is the host with a high degree and the highest

?betweenness centrality values at 17 and 2,496, respectively. The top-five nodes with the highest centrality values are shown in Table 2 and centrality values in Appendix 2. We can highlight that 78.06% of the nodes have grade 1 or 2 so they do not provide epidemiological information to the network but they may be peers involved in co-evolutionary processes.

Table 2. Rodentia network. The top-five nodes with the highest centrality values

Node	**Centrality values**		
	Degree	Betweenness	Closeness
Homo sapiens	53	18475.0	6.4×10^{-5}
Mus musculus	17	2496.5	6.3×10^{-5}
Andes virus	13	2003.5	6.3×10^{-5}
Rattus norvegicus	13	1362.6	6.3×10^{-5}
Cowpox virus	11	1869.2	6.3×10^{-5}

Community detection

Thirty-nine different communities were detected. Of which, 16 have two members and the largest group consisted of 32 members. This particular group included humans as shown in Appendix 2.

Subnetwork

Ten communities with at least eight members were selected in the subnetwork (Figure 2.B). We exclude of our selection the 1 and 9 communities because they are linear with common edges of a virus that influences the whole community for this reason they were not selected despite complying with the inclusion requirements.

Subcommunities

Three communities satisfied our selection criteria including community 3, 4 and 5. Community 3 acquiesced by 23 hosts and 11 viruses. This community was considered as a dense network as a number of links greatly exceeds the number of nodes (34 nodes and 55 links). In this community, only two viruses are non-zoonotic: herpesvirus 1 and cytomegalovirus (CMV3). Figure 2.C3 shows the gradient representing the number of viruses in each community host. It was noteworthy that *Myodes glareolus* is linked with the highest number of associated viruses (eight) and all of these are zoonotic.

In the fourth community, 32 nodes and 33 links were observed. Within this sub-community, 16 rodent species were recognized along with 16 viruses, in which only one virus was not zoonotic (Gbagroube). Figure 2.C4 highlighted the proximity of *Peromyscus maniculatus* to the human nodes indicating a large number of shared viruses. On the other hand, community 5 consisted of 20 nodes and 19 links representing six rodent species and fourteen viruses. Of these viruses, only two viruses of this community are zoonotic: Lymphocytic Choriomeningitis virus (LCV) and California Encephalitis virus. In this sub-community, most viruses linked only with *Mus musculus*.

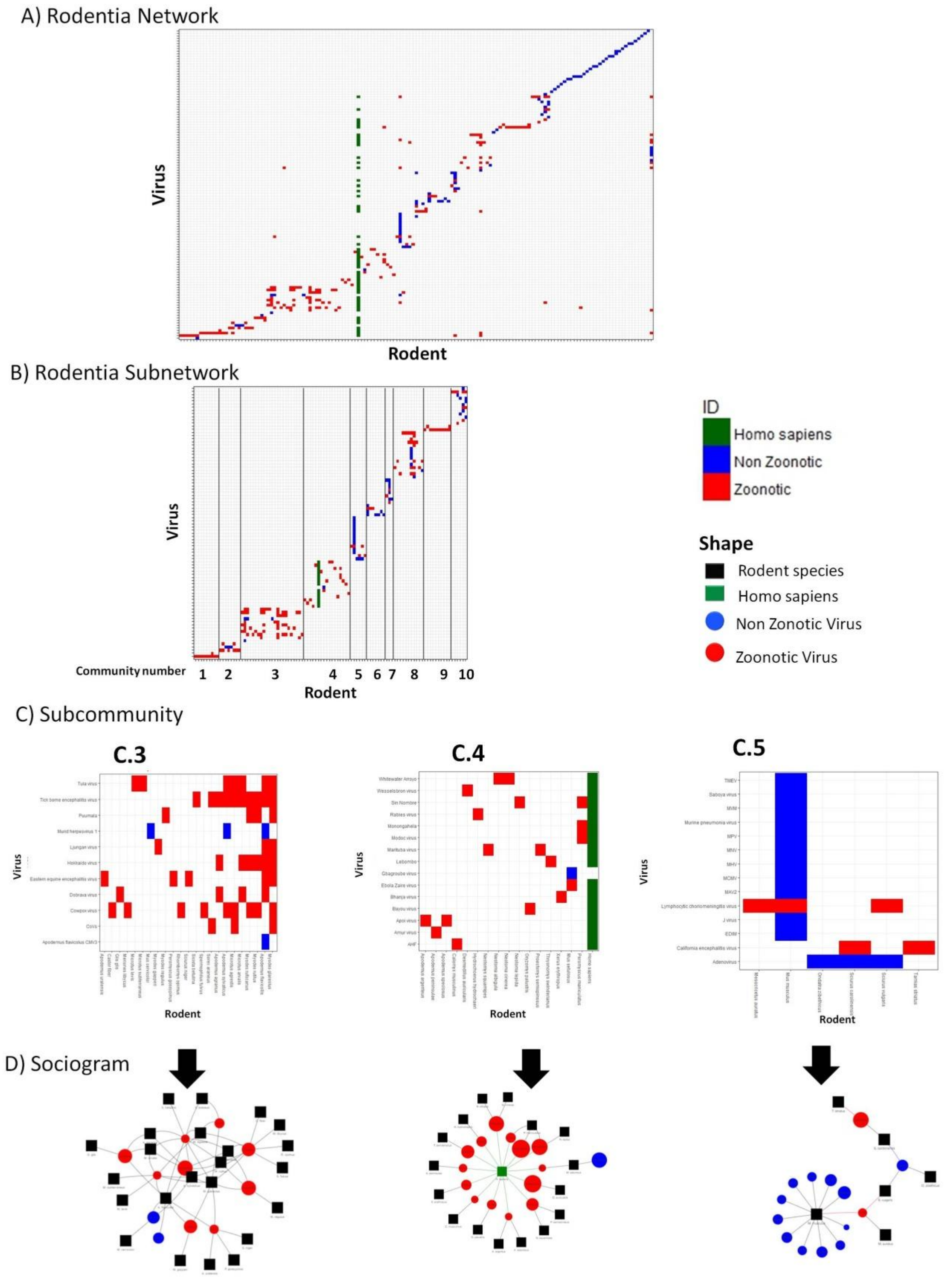

Figure 2. Rodentia networks. A) Whole Rodentia network B) Subnetwork, with 10 selected communities, renamed with a consecutive number. Lines were added to separate the communities C) Subcommunities selected to show the host-species interactions; D) Sociogram to facilitate the visualization of the interactions.

Host-Host Rodentia Network

In this particular network, 147 nodes of rodent species were present with 502 links. In the case of the diameter, the network had a value of 5 and the density was 0.0627 (Figure 3.A). On the other hand, the top-five nodes with the highest centrality values are shown in Table 2 and the remaining values in Appendix 3. In our community detection, 35 different communities were detected. Finally, the largest community contained 43 members followed by a group of 21 members as shown in Appendix 3.

Virus-Virus Rodentia Network

In the network of virus-virus, 122 nodes and 1,661 links were identified. In addition, the diameter and the density of the network were 4 and 0.3494, respectively (Figure 3.B). Whereas, the top-five viruses with the highest centrality values are all zoonoses (Table 3). Eventually, fifty-three different communities were detected. In this case, the largest group was noted with 52 members and the second highest community was found with only 12 members. Ultimately, all the centrality values and community detection are attached in Appendix 3.

Table 3. Top-five nodes of rodents network with the highest centrality values in the collapsed network.

Network	**Node**	**Centrality values**		
		Degree	Betweenness	Closeness
Host-Host	*Homo sapiens*	105	4932.8	2.1×10^{-4}
	Rattus rattus	35	443.7	2.1×10^{-4}
	Rattus norvegicus	30	293.6	2.1×10^{-4}
	Myodes glareolus	26	111.8	2.1×10^{-4}
	Apodemus sylvaticus	21	75.3	2.1×10^{-4}

Virus-Virus	Venezuelan Equine Encephalitis Virus	76	516.6	3.0 x 10^{-4}
	Encephalomyocarditis Virus	70	181.2	3.0 x 10^{-4}
	Severe Fever With Thrombocytopenia Syndrome	69	203.1	3.0 x 10^{-4}
	Eastern Equine Encephalitis Virus	68	202.8	3.0 x 10^{-4}
	Lymphocytic Choriomeningitis Virus	65	171.5	3.0 x 10^{-4}

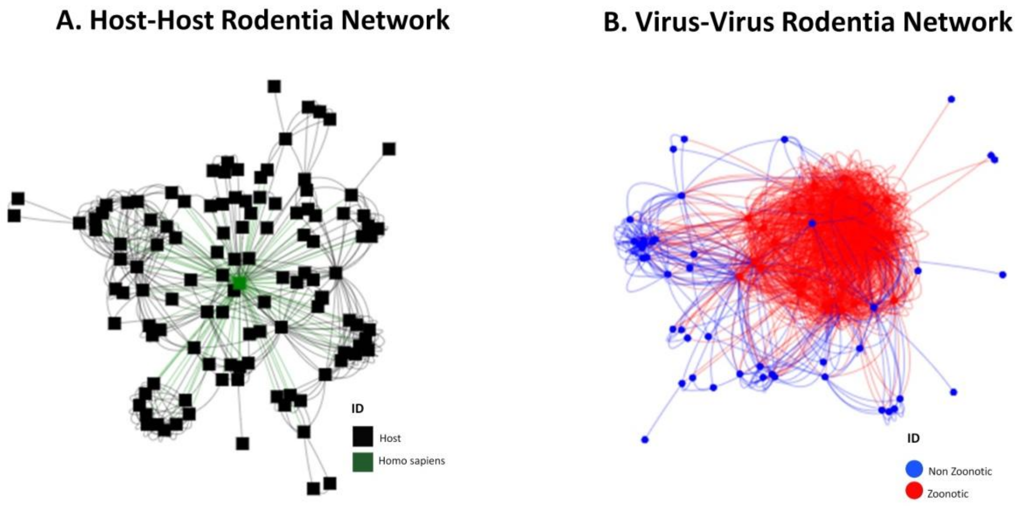

Figure 3. Collapsed networks A) Host-Host Rodentia Network; B) Virus-Virus Rodentia Network.

Chiroptera network

Overall Networks Analyzes

A total of 387 nodes and 736 links were observed in the bat network. Regarding the network diameter was 10 and the density was 0.0049 (Figure 4 A). As well, three zoonotic viruses headed the list with the highest values of degree and betweenness. These are bat coronavirus, rabies and bat paramyxovirus (Table 4). We can also highlight that 65.71% of the nodes have grade 1 or 2 so they do not provide much information to the network but they may be peers involved in co-evolutionary processes. All centrality values are attached in Appendix 2

Table 4. Top-five nodes of Chiroptera network with the highest centrality values.

Node	**Centrality values**		
	Degree	Betweenness	Closeness
Bat coronavirus	80	26930.5	2.8×10^{-4}
Rabia	56	15539.7	2.6×10^{-4}
Bat paramyxovirus	55	13920.7	2.7×10^{-4}
Homo sapiens	39	13233.5	2.7×10^{-4}
Astrovirus	31	4857.4	2.6×10^{-4}

Community detection

Twenty-nine different communities were detected. In this case, four communities had only two members and the largest community contained 38 members as shown in Appendix 2.

Subnetwork

Eleven communities consist of eight memberships or higher (Figure 4B). First, in the community 1, 3 and 4 are linear and possess simple edges with a virus that influences the whole community. Second, the community 7 is a homogeneous community with rich ecological interactions but not highly related to zoonotic viruses. The last community is associated with humans with the highest number of zoonotic viruses involved, showed in the Figure 4.C and 4.D. and detailed in the next section.

Subcommunities

A low number of zoonotic viruses were found in homogeneous bat networks communities, we only focus on the community where the human node was included. As shown in figure 4 A, three red lines representing the three highly connected viruses in the network followed by a homogeneous community and later in green the human node connections.

The human-community (Figure 4.C and 4.D) has 13 host nodes (including human) and 23 virus nodes with 45 links. One could also say that, the Fruitbat parvovirus is the only member that has not being recognized as zoonotic. Finally, we emphasized that the presence of the Minioterus, Mormopterus and Saccolaimus bat genera is only for direct viral sharing with humans.

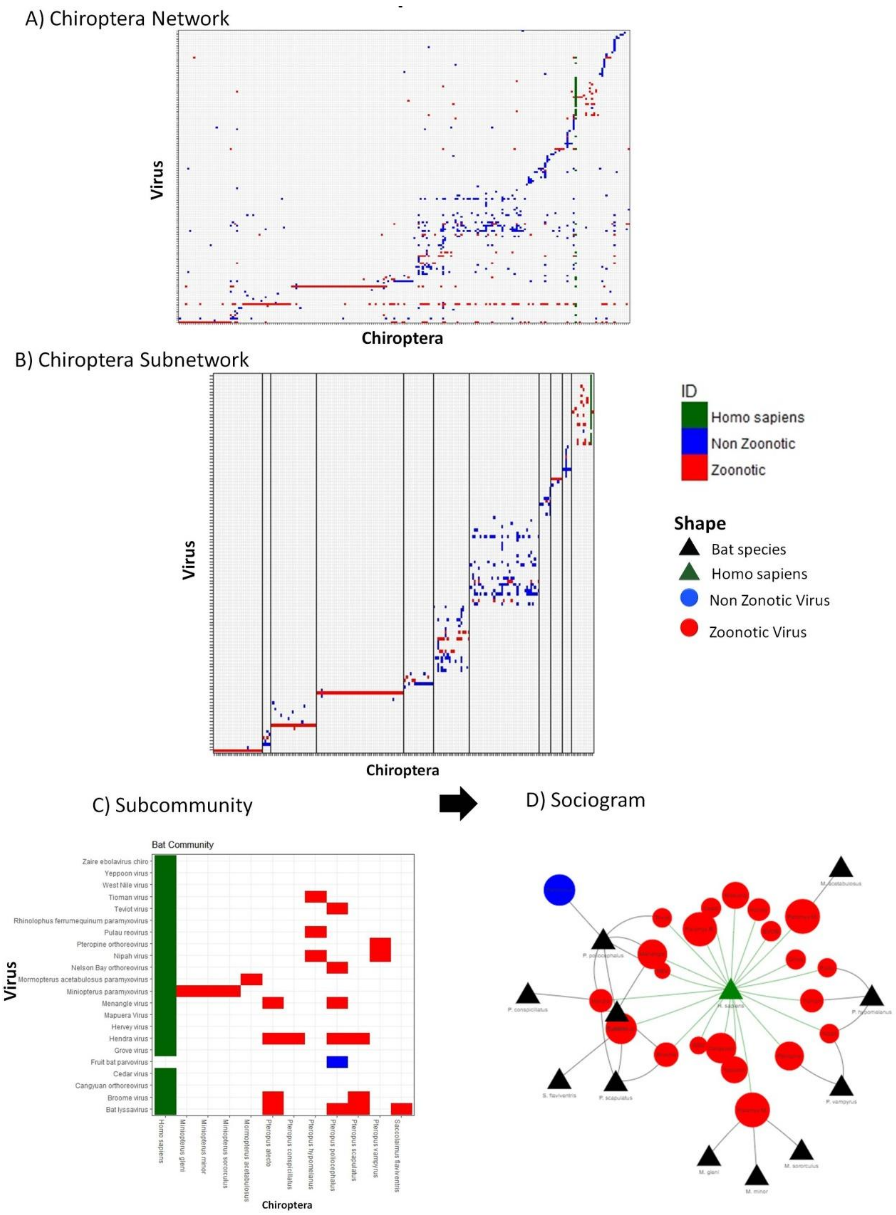

Figure 4. Chiroptera networks A) Chiroptera host-virus network, B) Subnetwork, with 11 communities selected. Lines were added to separate the different communities to observe their composition, and detect the relevant communities; C) Human subcommunity selected to show the host-species interactions; D) Sociogram to facilitate the visualization of the interactions.

Host-Host Chiroptera Network

The host-host Chiroptera network contained 221 nodes and 6,949 links. While the diameter and the density of the network were 5 and 0.2911, respectively (Figure 5.A). Additionally, the top-five nodes with the highest centrality values are shown in Table 5 and detailed results in Appendix 4. On the other hand, sixty-seven different communities were detected; the largest one was recognized with 69 members. The subsequent community consisted of 56 members including human node (Appendix 4).

Virus-Virus Chiroptera Network

In this network, 164 nodes were observed with 2,132 links. In addition, the diameter of the network was 4 and the density was 0.1655 (Figure 5.B). In Table 5, three coronaviruses headed the list (Bat coronavirus, alphacoronavirus and betacoronavirus), along with two other viruses. Certainly all of them are zoonotic (Appendix 4). One could also say that ninety-seven communities were detected. On this occasion, the largest community was identified with 35 viruses, all of them zoonotic (Appendix 4).

Table 5. Collapsed Chiroptera network. The top-five nodes with the highest centrality values

Network	**Node**	**Centrality values**		
		Degree	Betweenness	Closeness
Host-Host	*Homo sapiens*	181	1556.6	8.2×10^{-4}
	Myotis daubentonii	174	767.5	8.2×10^{-4}
	Glossophaga soricina	155	610.8	8.3×10^{-4}
	Rhinolophus ferrumequinum	146	484.6	8.0×10^{-4}
	Desmodus rotundus	138	873.4	$8. 2 \times 10^{-4}$
Virus-Virus	Bat coronavirus	138	2402.0	1.3×10^{-3}
	Bat paramyxovirus	110	917.9	1.2×10^{-3}
	European bat lyssavirus	90	376.8	1.2×10^{-3}
	Betacoronavirus	85	581.9	1.2×10^{-3}

Alphacoronavirus	77	358.7	1.2×10^{-3}

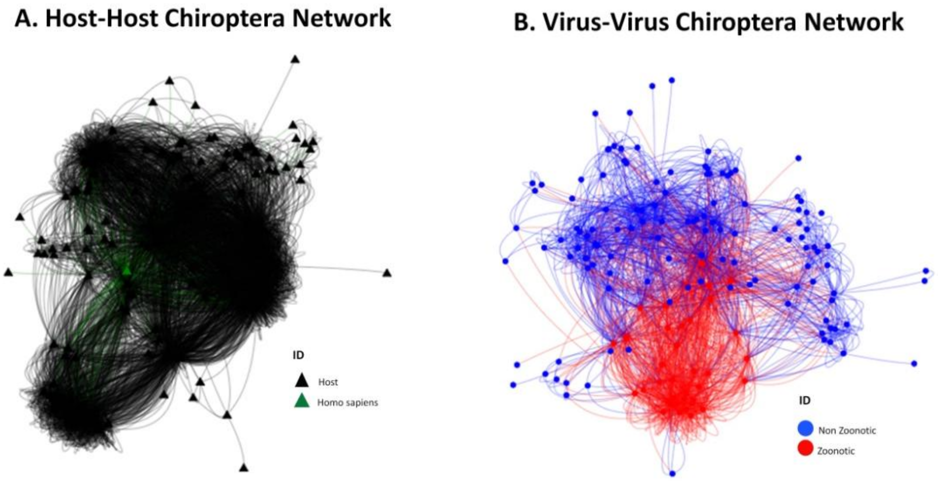

Figure 5. Collapsed networks A) Host-Host Rodentia Network; B) Virus-Virus Rodentia Network.

Discussion

Bats are well-known as excellent reservoirs for zoonotic viruses that usually result in high public health impact (Gay et al., 2014; Luis et al., 2013, 2015; Plowright et al., 2015). Nevertheless, in our database, 43% of the rodent's viruses are zoonotic whereas the proportion in bats is roughly half (24%) compared to rodents. Thus, rodents should not be overlooked. However, bats are more linked to more cosmopolitan viruses with broad distributions in the hosts.

In the bipartite networks of bats, the principal actors (top values of degree, betweenness, and closeness) were all viruses, including bat coronavirus, rabies, bat paramyxovirus and astrovirus (Table 4). On the other hand, the principal actors in the rodent bipartite network were two host species (*Mus musculus* and *Rattus norvegicus*), and two viruses (Andes virus and Cowpox virus) (Table 2). Hence, the bat viruses possess a higher degree of connectivity with a large number of bat hosts.

The ratio of nodes to edges in bats was observed at 1:1.9. It indicates that among bats, viruses and hosts are shared in a higher degree, due to the presence of the cosmopolitan viruses in a large number of bat species. In other words, one bat species may interact with a high number of viruses or one virus is detected in many different bat species.

Luis et al. (2015) also built viral association networks in the orders Rodentia and Chiroptera. Although they use the centrality metrics as a response variable in a Generalized Linear Model to recognize the phylogenetic, functional and ecological characteristics those give them this high connectivity. Both works with different approaches reach the same conclusion: the viruses associated with bats are shared twice more than among rodents.

The pattern of bat virus associated with a higher diversity of host than in rodent viruses has been observed in viral metacommunities with different spatial scale analysis (Nieto-Rabiela *et.al*, 2018). In contrast, the same ratio in rodents was observed at 1:1.2. This observation suggests a specific one-to-one union, a virus to one host and a host to one virus. Therefore, a rodent's network with more divisions is shown. This may associate with the dispersion capacity that each order has. The ratio in bats is higher due to their flight capacity (Wang, Walker, & Poon, 2011). However, studies on viruses detected in others mammals have not yet been developed at the large scale. Therefore we cannot conclude that sharing viruses is the key feature of bats. We only detected the differences between bats and rodents.

In collapsed host-host networks in both bats and rodents, the human node is closely linked with the species that host zoonotic viruses. The largest community starring human node is surrounded by three to four smaller groups in both networks. We can highlight that in the largest community where the human is host species with high adaptability, large distribution and without phylogenetic distinction. Also, the closest hosts to the human node are the great reservoirs of hantaviruses, rabies, dengue then the damage that they can cause is potentiates. However, the clusters in the bat network are four times denser compared to rodents; this makes it easier to continue sharing the viruses. In addition, they can act as virus mixers and acquire characteristics that turn them into zoonotic or that infect other species. Besides, the human node is more closely connected to bats. It shows that viruses are shared to a greater degree among bats as discussed earlier (Figure 3.A and 5.A). The plausible explanation is that different species of bats live in a close proximity, especially in the caves. Indeed, a larger number of bat species are always observed in the same space (Kerth, Perony, & Schweitzer, 2011).

The difference in the connectivity between the orders, change the zoonotic potential of which one. Because high connectivity facilitate the viral transmission between the specie and between other species. We can highlight the relevance of the bat capability to disperse them.Interestingly, we found *Glossophaga soricina* with the highest closeness value in the host-host network despite the fact that only three viruses of this specimen have been isolated: bat coronavirus, bat paramyxovirus, and rabies. This is because these three viruses have a high viral diversity and when the network collapses *Glossophaga soricina* connects directly with 155 hosts, being the central node even over the human. This suggests that this species is prone to harbor several viruses. However, ecological and physiological reasons driving this pattern are still unknown.

In both virus-virus networks, we similarly observed some large groups that include all the zoonotic viruses. The grouping of zoonotic viruses suggests a high capacity for mutation and adaptability to different hosts. For that reason, the viruses are shared among different hosts and thus intricate communities are presented (Woolhouse, 2001). In bats, these clusters are disordered and close together resulting in a broad viral exchange among bats. In contrast, a closer relationship was observed in rodent viral-viral network indicating smaller groups around zoonotic viruses. It’s difficult though to compare on our virus-virus network to other works as most studies focus on the hosts. Moreover, we faced deficiencies in the knowledge on the organization of the viral communities, assembly rules, co-occurrences or even cross-antigenicity. These issues directly affect our network architectures. For that reason, deeper comprehension is required to unravel this entanglement.

One of the objectives covered in this work was to recognize non-zoonotic viruses that may strongly connect with humans indicating their zoonotic potential. In the bat-virus community where human is involved, we found bats with distribution in Africa and Australia due to their megadiversity and therefore high contact rates human-wildlife (Picker & Samways, 1996).

In addition, we detected the presence of one non-zoonotic virus in this human-community is fruitbat parvovirus. Basically, parvoviruses were transmitted from bats to other mammals by a viral ancestor suggesting their zoonotic capacity (Canuti et al., 2011). Besides, groups of genes in their genome denote this potential. Even though the virus is currently rooted in bats (Canuti et al., 2011). It firmly connected with the human in our network by *Pteropus poliocephalus*, an endemic species of Eastern Australia (Lunney, D., Richards, G. & Dickman, 2008). Future studies are recommended to elucidate its potential.

Andes viruses (rodents), Cowpox (rodents) and rabies (bats) were defined as main actors (with high values of degree, betweenness, and closeness) in the bipartite networks. However, their importance disappeared when the networks was collapsed as virus-viruses interactions. Because their geographical restriction may limit their viral connectivity. Andes virus is only distributed in South America (Martinez et al., 2005), Cowpox in Europe (Vorou, Papavassiliou, & Pierroutsakos, 2008) and rabies in America (Moratelli & Calisher, 2015). Therefore, these viruses were less important in the virus-virus networks compared to the worldwide distributed ones so subsequent works must be analyzed at geographical scales.

Coronaviruses in bats have always stood out in both, bipartite and collapsed networks in terms of connectivity, with high values of degree, betweenness, and closeness. In this case, three most prominent coronaviruses are bat coronavirus, alpha coronavirus, and beta coronavirus. Also, each virus is a protagonist in their own community. These are RNA viruses with high mutation rate, besides, the viruses possess great plasticity allowing them to horizontally transfer accessory genes which facilitate new host and niche establishment (de Groot et al., 2011).

In the rodents community selected, the community 3 has members with predominantly Europe distribution. Further, two non-zoonotic viruses are between nine zoonotic viruses, but they do not suggest us zoonotic potential because they do not have direct contact with the human. Therefore, in this community we do not find viruses with zoonotic potential.

In the rodent community 5, *Mus musculus* have high values of connectivity but in the sociogram (Figure 2.D); we can see that the connectivity is with non-zoonotic viruses. For that, it loose relevance in public health but is relevant for disease ecology. In addition, two zoonotic viruses are inside the community, but they can suggest us the capability to change the other viruses to zoonotic using the *M. musculus* as a virus mixer. However, we do not consider it because the proportion of zoonotic virus is low, adding the specificity of rodents' viruses and the associative characteristics founding in the rodents. Is to say, the union one-to-one developed in this research that difficult the spillover but does not prohibit.

In the human-rodent community, Gbagroube virus is noteworthy as the unique non-zoonotic virus found in the community. However, the genetics of Gbagroube virus is similar to Lassa virus which is a deadly zoonoses in humans (Coulibaly-N'Golo et al., 2011). In conclusion, Gbagroube virus is potentially adaptive to infect human, because it has genetic similarity to Lassa virus (Coulibaly-N'Golo et al., 2011), strong connection with other zoonotic viruses and human. Also Gbagroube virus should be closely monitored and its host: *Mus setulosus* with distribution in the central part of Africa (Granjon, 2016).

In our study, the human is the most relevant and largest node connected in both groups. The relevance of the human in the network is explained by different factors. First, human overpopulation and globalization have been pushing people to invade every place on earth and facing high possibility to contact with innumerable organisms resulting in zoonotic emerging diseases (Kock, 2014). Second, anthropocentrism is completely unavoidable. Science is created from the human point of view and with emphasis on the interaction between ecosystem and human being (Laguna, Marcelín, Patrick, & Vázquez, 2016). Therefore, we intend to search for zoonoses rather than diseases without relevance in public health, what could inevitably have biased our results.

In the database, we do not have Ebola reports because in the database of DBATVIR do not identify the host species where the virus was isolated. Similarly, we found 78.06% in rodent nodes and 65.71% in bats nodes poorly connected (1-2 degree). Surely, bats have associations that we do not recognize. In addition, there are actual impossible associations but we do not know, because there is a deficiency of true negatives records. We highlight the relevance to report negative samples and the number of animals in meticulous informs.

A future study may complement and compare our study with models where the influence of the humans is omitted. We must take into account that human node influences the network structure. In spite of this, the ecological relationships must be analyzed without this influence. Surely more lax networks will be observed for the decrease of this anthropocentric force. However, our study does need to include both to identify potentially zoonotic viruses.

It is pertinent that, in future investigations, different characteristics of the viruses must be considered simultaneously and not only by their connectivity in the network such as gene sequence, type of transmission, virulence, etc. In the present study, we only focus on viral hosting capability, not on the symbionts and their associative nature. Spatial analysis may help to elaborately explain our findings in any particular regions of the world.

CONCLUSIONS

Graph theory is an excellent tool to understand and recognize host-virus associations. However, it is not always exploited its maximum potential and often only appreciated for its visual aspect without deepening the background of the values and connection types.

Rodents should be taken into account as important reservoirs for zoonotic viruses. At least in our database, a greater proportion of zoonotic viruses were addressed. Fruitbat parvovirus and Gbagroube virus in rodents should be monitored to elucidate their zoonotic potential. In the present study, we only assessed through their network proximity to humans and other zoonotic viruses. Then, molecular genetics approaches may help to confirm our results. The counting of zoonotic simbionts in each order is not a conclusive estimate of their zoonotic potential, our findings reveal that viruses were more frequently shared among bats than rodents. For that reason, bats have more zoonotic potential that the rodents. However, potential emerging zoonotic diseases may arise from both taxonomic groups. These mammals should be closely watched to set an early alarm once the viruses' spillover.

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Conflict of interest

We declare that we have no conflict of interest.

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Conclusiones

Con respecto a la Teoría de Metacomunidades podemos resaltar como ventajas, que nos permite detectar orden conforme a los gradientes analizados y por ende estructuras que nos sugieren procesos ecológicos que rigen o predominan a ciertas escalas, expresando tales ordenamientos. Por lo que podemos entender de mejor manera las dinámicas ecológicas analizadas. Sin embargo, el elegir la escala espacial es complicado, depende mucho de la pregunta a responder y aun así, se deben asumir o tomar supuestos para poder delimitar una escala.

Por otro lado, en la Teoría de Grafos como fortalezas encontramos que se pueden analizar de manera sencilla la cercanía de los virus a los humanos, que nos sugieren potencial zoonotico, podemos detectar grupos por su cercanía, evaluar o valorar que tan fuertes son las conexiones y analizar cada parte del sistema, cada hospedero y/o cada virus. Sin embargo es muy difícil evaluar características filogenéticas, funcionales u ordenamiento dentro de la red, por lo que se analizan con otros métodos diferentes a la teoría de redes.

Tomando en cuenta los puntos anteriores la mejor forma de analizar estos sistemas virus-hospedero es utilizando ambas teorías, combinándolas y aprovechando las ventajas que nos ofrece cada una. Es decir, la teoría de grafos nos permite entender cada parte y detalle, además de mostrarnos los grupos naturales, los cuales pueden ser tomados como las escalas en el análisis de metacomunidades donde podemos entender mejor los procesos ecológicos que los organizan.

Más concretamente tenemos las preferencias de asociación de los virus en las escalas en las cuales se trabajaron, por ejemplo en norteamerica sabemos que es más fácil que los virus se asocien a roedores cercanos filogenericamente que a roedores con historias de vida similares, esto facilita el monitoreo y la búsqueda de hospederos reservorios de virus.

También resaltamos la importancia de monitorear a Gbagrouvirus y el Parvovirus del Murciélago frugívoro, ya que estos virus los encontramos en nuestra red muy cerca de virus zoonoticos y aun más importante del humano, sugiriéndonos su potencial zoonotico y al referirnos a la literatura encontramos reportes de su semejanza genética con virus zoonoticos, al conjuntar esta información proponemos un monitoreo exhaustivo a estas dos especies.