



DEPARTAMENTO DE
MICroBiologia
UNIVERSIDADE DE SÃO PAULO



Arboviroses

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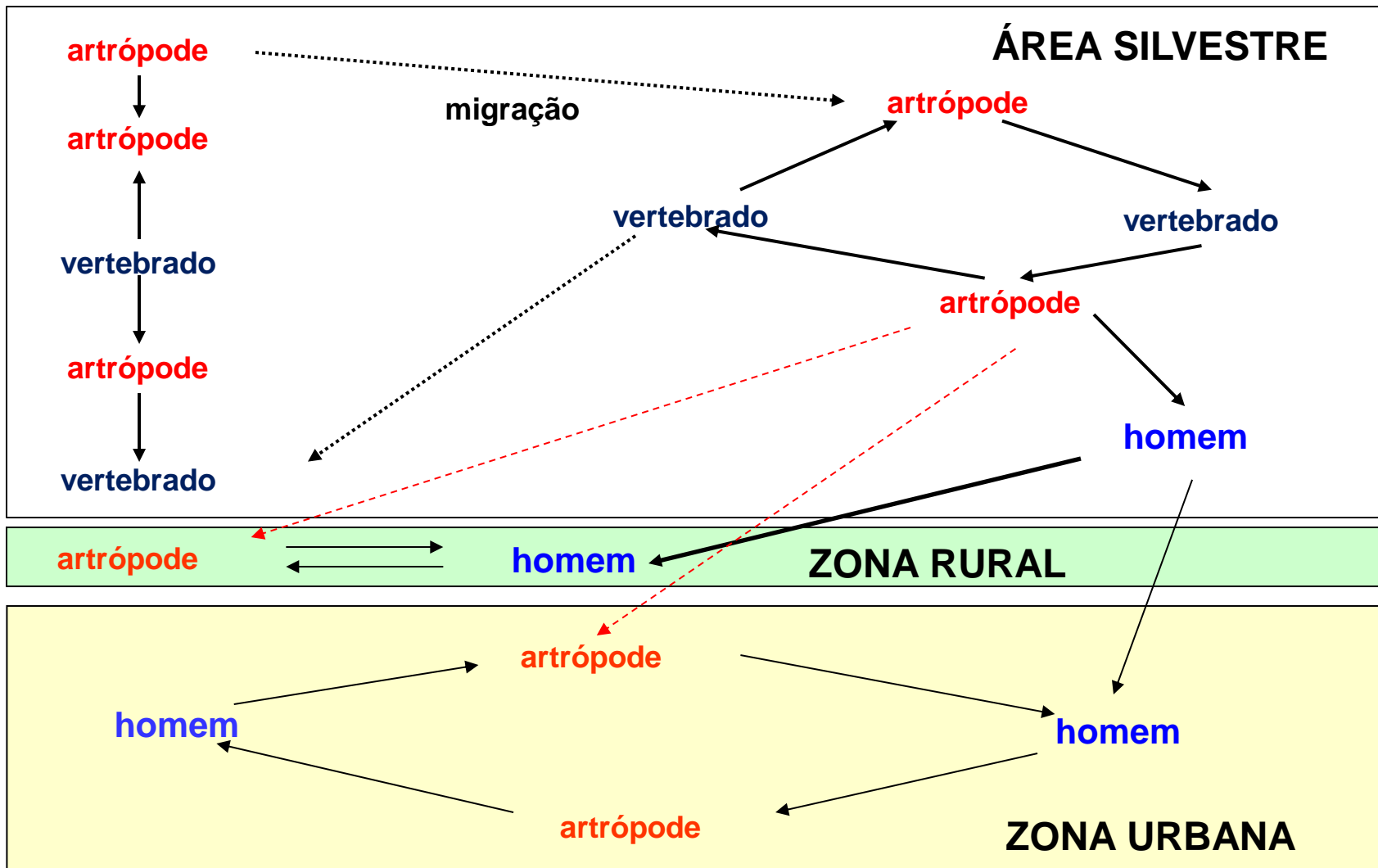
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Arboviroses

ARBOVÍRUS: arthropode-borne viruses

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Ciclo de transmissão



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Família *Flaviviridae*

- Conhecida desde o início do século.
- Seu primeiro membro, o vírus da febre amarela (YF), foi reconhecido como um agente filtrável, em 1927.
- O nome tem origem na palavra latina *flavus* = amarelo.
- Possui quatro gêneros (60 espécies), com vírus que infectam humanos e animais:
 - Flavivírus
 - Pestivírus
 - Hepacivírus
 - Pegivírus

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O gênero *Flavivírus*

- Pelo menos 73 sorotipos ≠, 40 já foram associados a doenças humanas.
- Os mais importantes são:

Dengue 1
Dengue 2
Dengue 3
Dengue 4

Sorogrupo DEN
62 a 77% de identidade

Febre amarela

→ Sorotipo único

West Nile
Encefalite de Saint Louis
Encefalite Japonesa

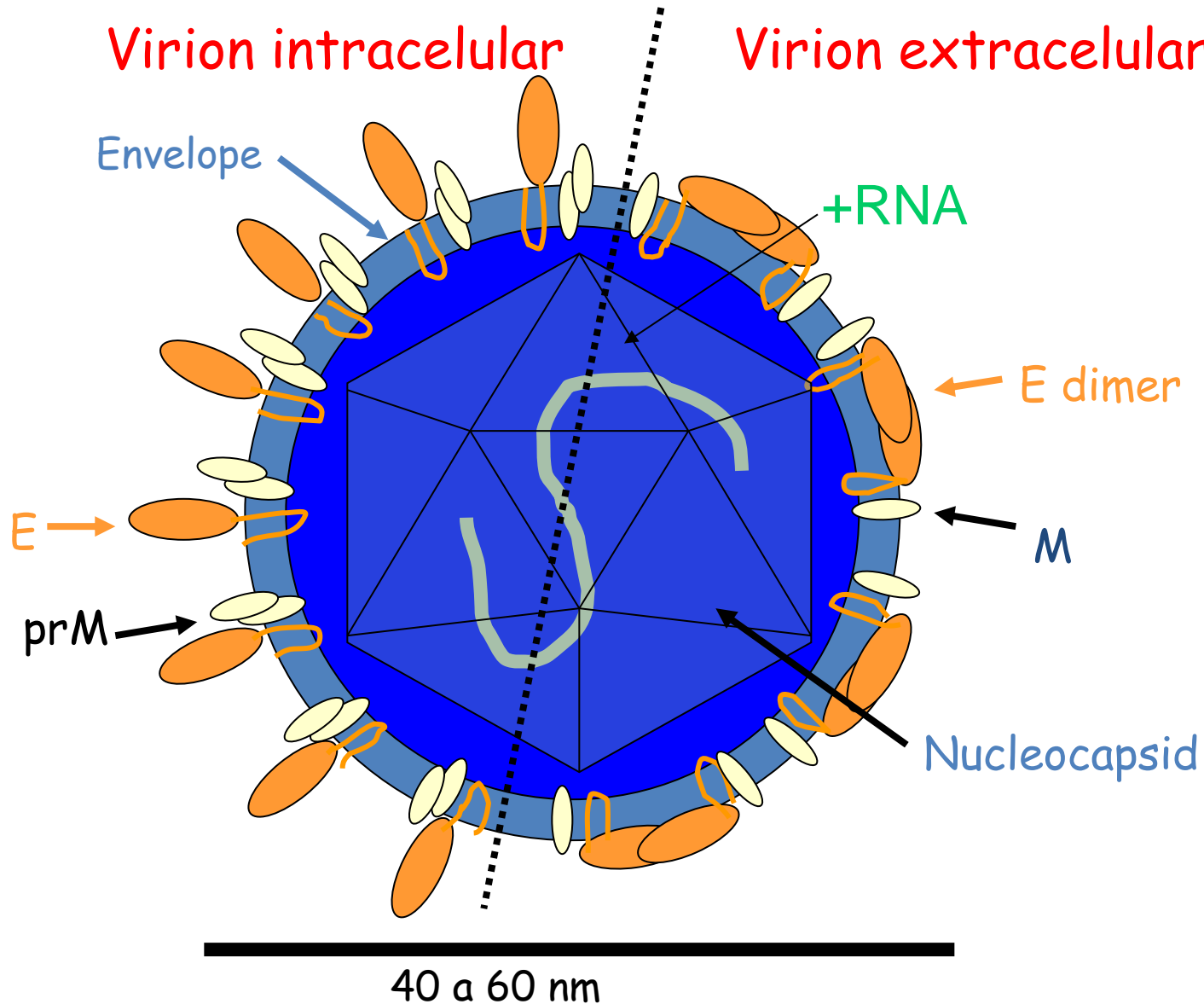
Sorogrupo JE
72 a 93% de identidade

“Tick-borne” encefalite

→ Sorogrupo TBE
77 a 96% de identidade

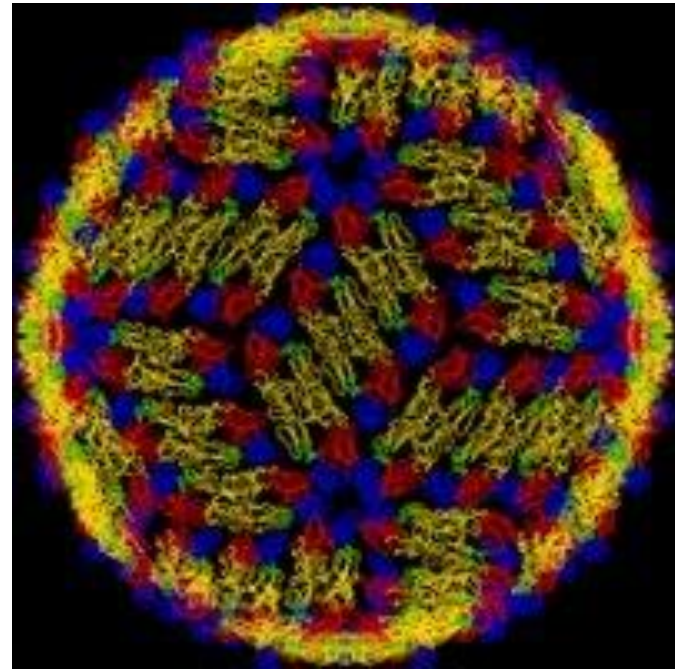
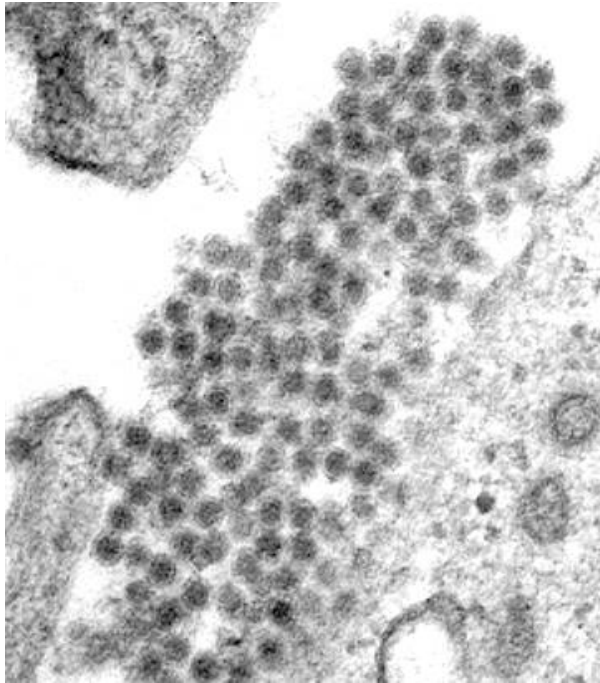
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Flavivírus: Estrutura da partícula viral



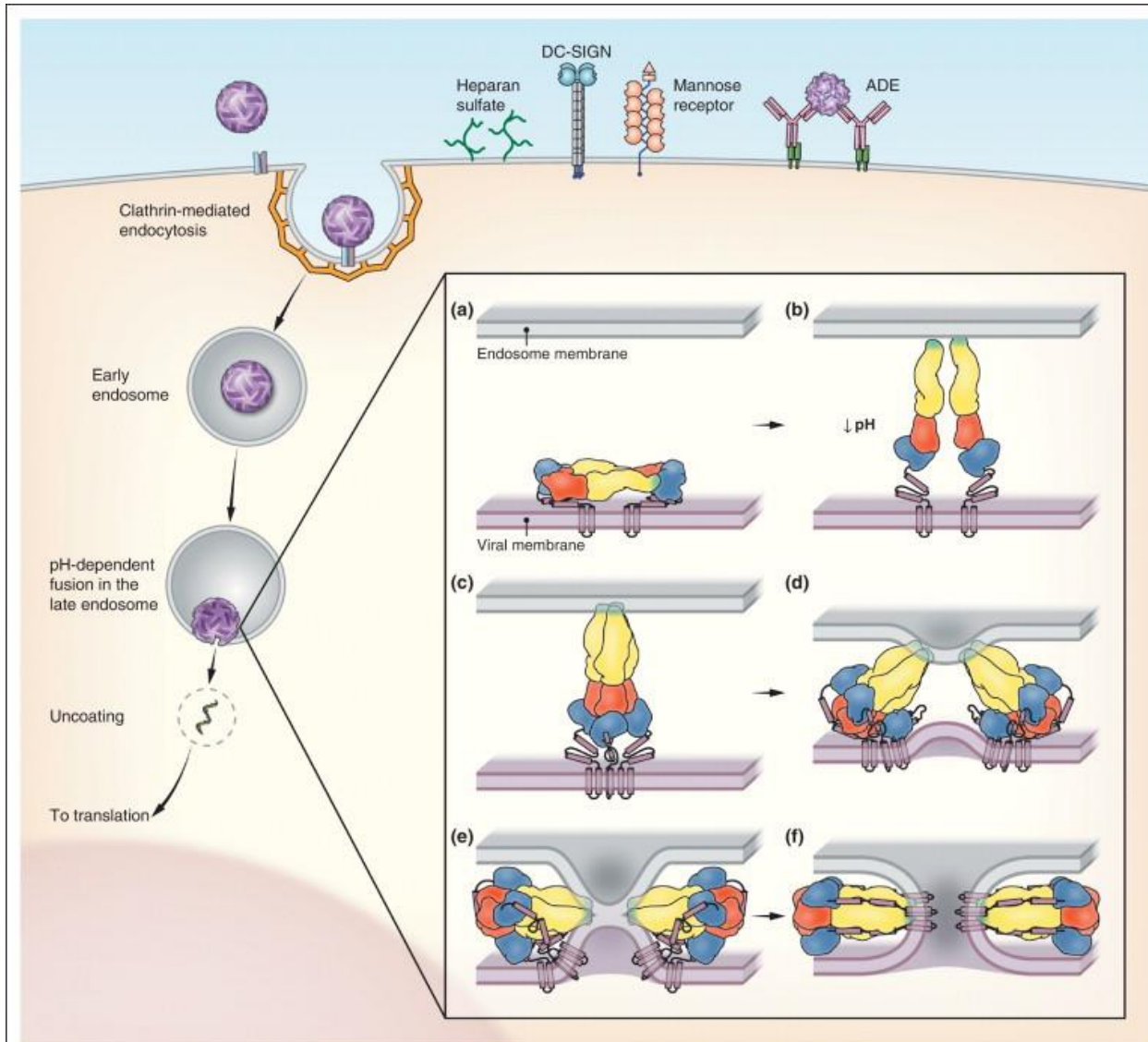
Arboviroses

Flavivírus: Estrutura da partícula viral



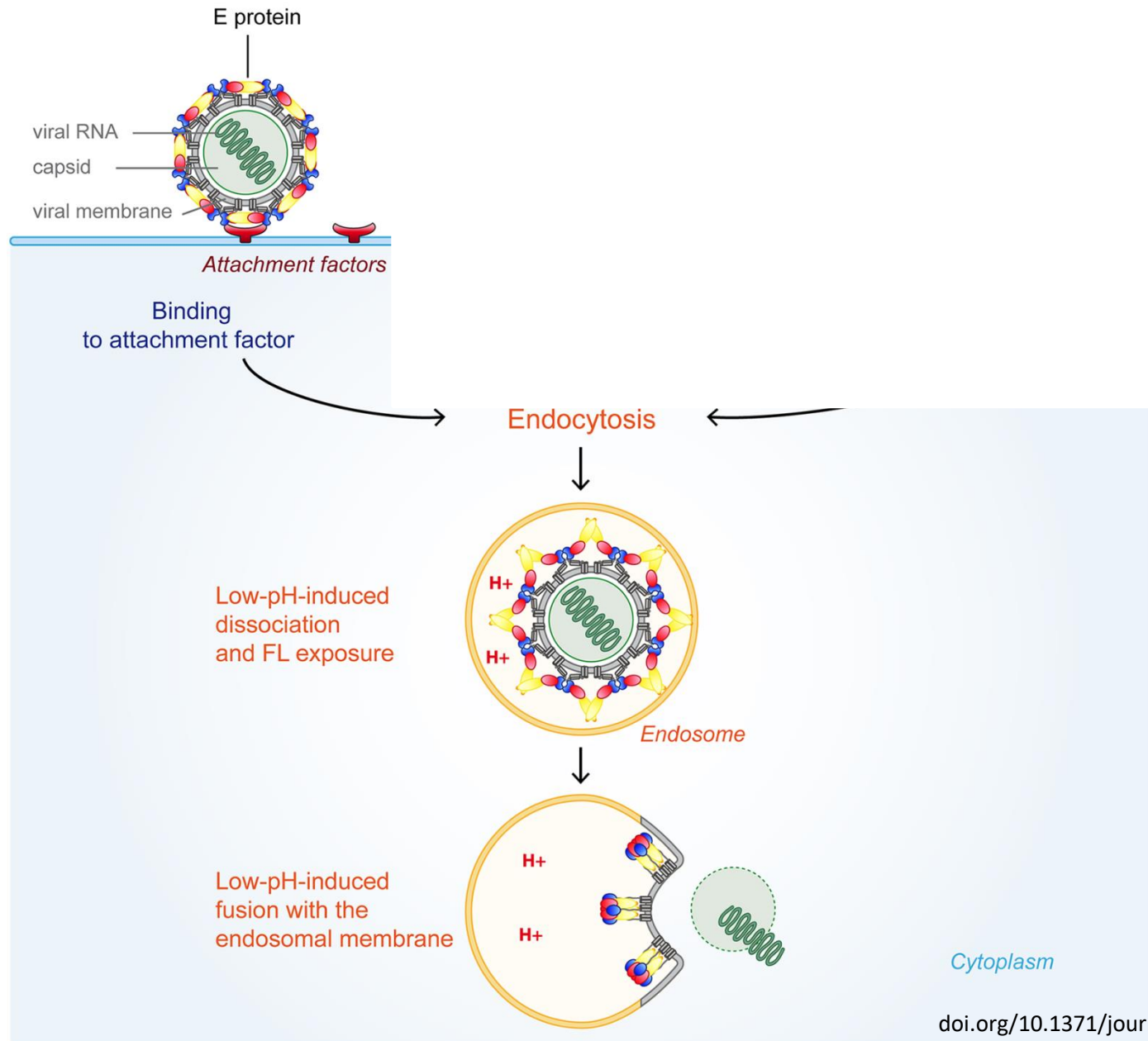
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Flavivírus: Entrada da partícula viral



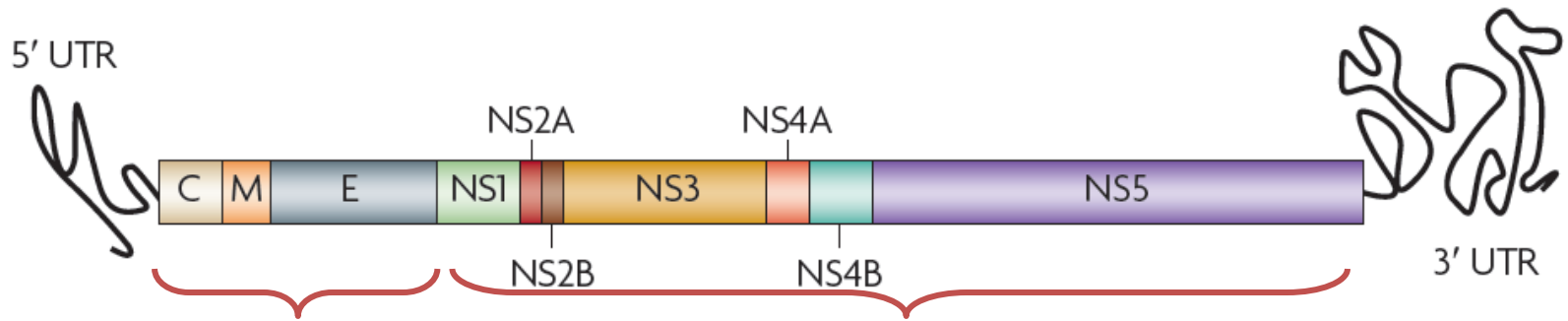
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Flavivírus: Entrada do vírus



Febres hemorrágicas virais

Genoma dos *Flavivírus*

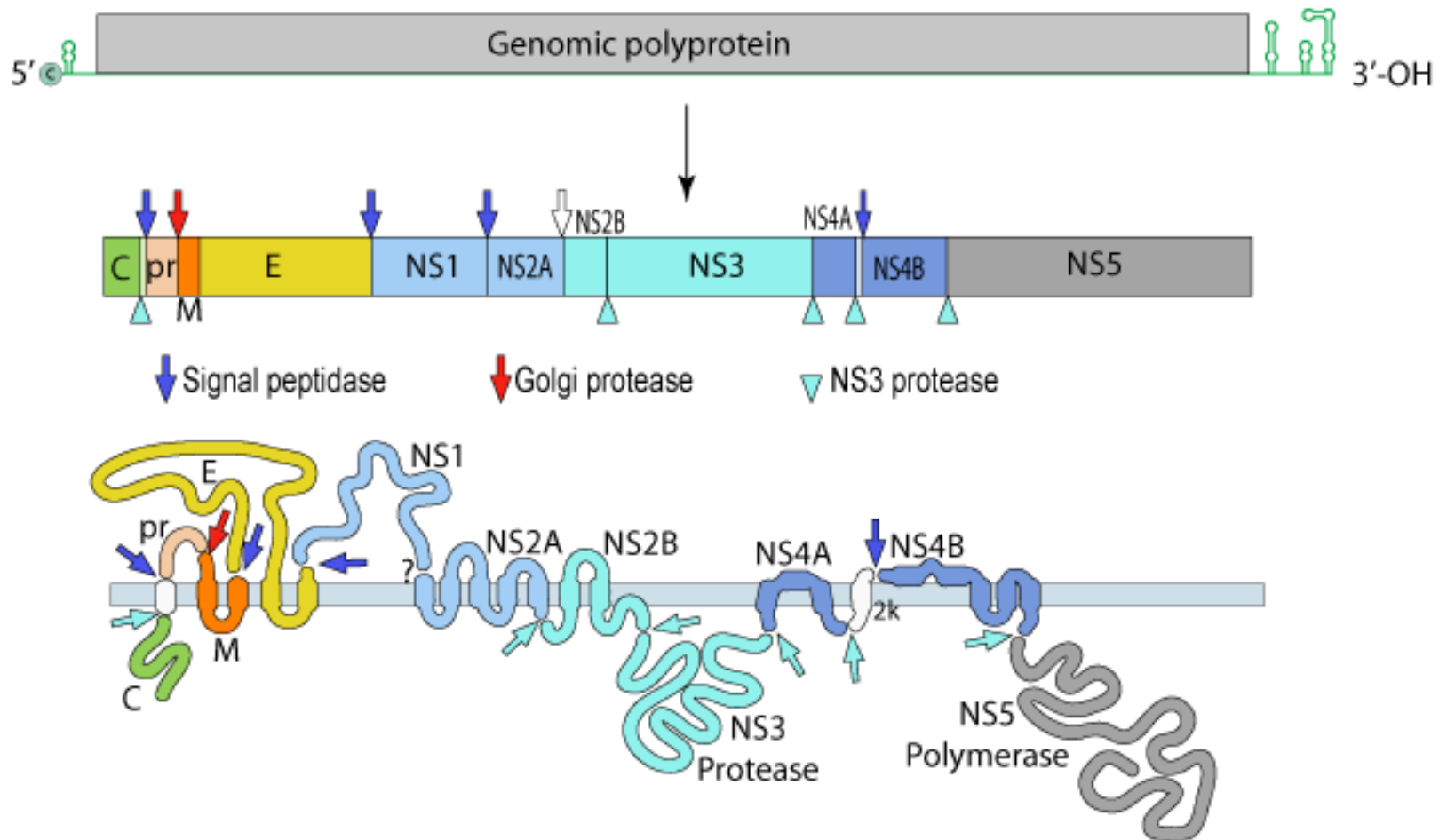


Três genes que codificam para proteínas estruturais

Sete genes que codificam para proteínas não estruturais

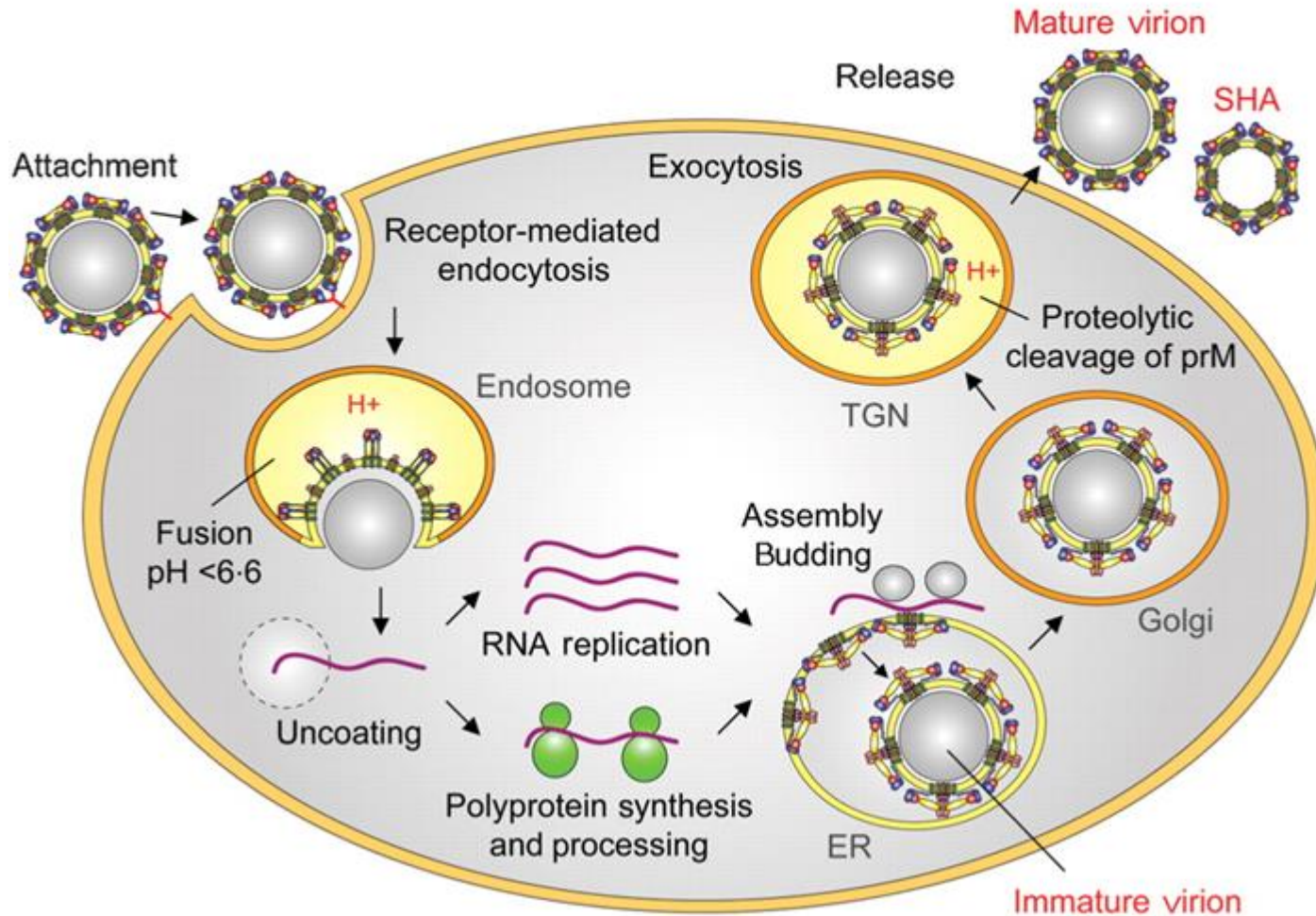
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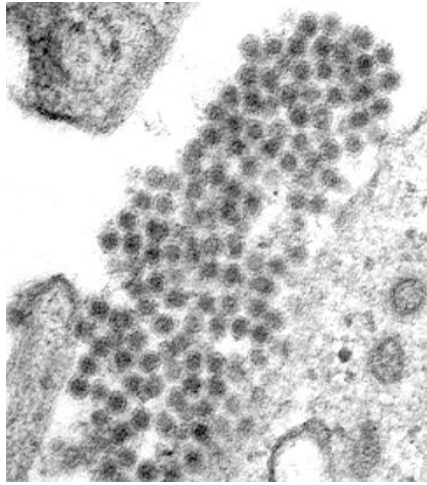
Genoma dos *Flavivírus*



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Replicação dos Flavivírus





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Febre amarela

Dengue

Família: *Flaviviridae*

Gênero: *Flavivírus*

Transmissão: vetor artrópode - *Haemagogus janthinomis* e *Aedes aegypti*

Hospedeiros: *Silvestre - macacos; Urbano - homem*

Partículas virais: Esféricas 45 nm, envelopadas

Proteínas estruturais: glicoproteína E ; nucleoproteína: C; membrana: M

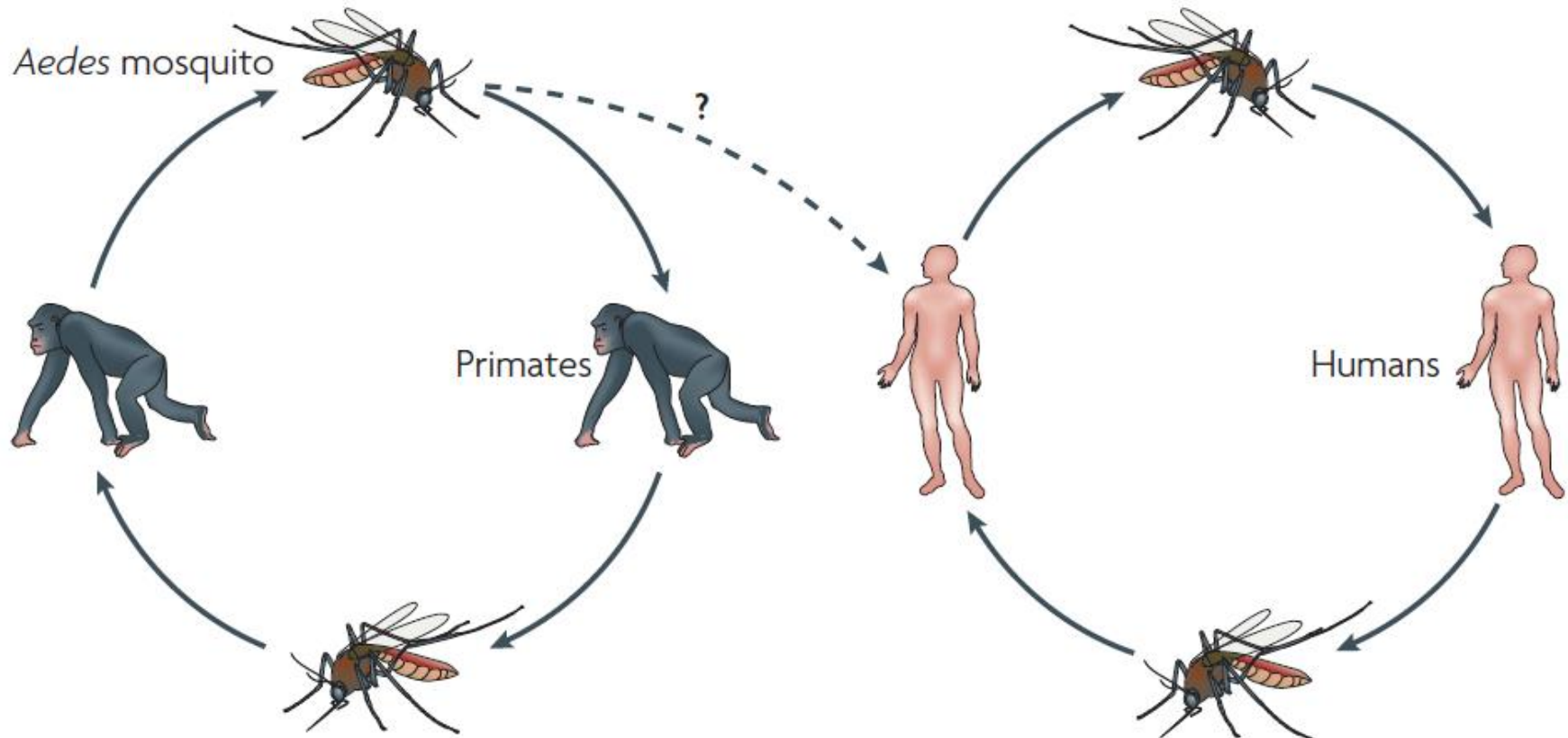
Genoma: ss-RNA polaridade positiva

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Replicação e transmissão do DENV, YFV (e outros arbovírus)

Sylvatic/enzootic

Epidemic

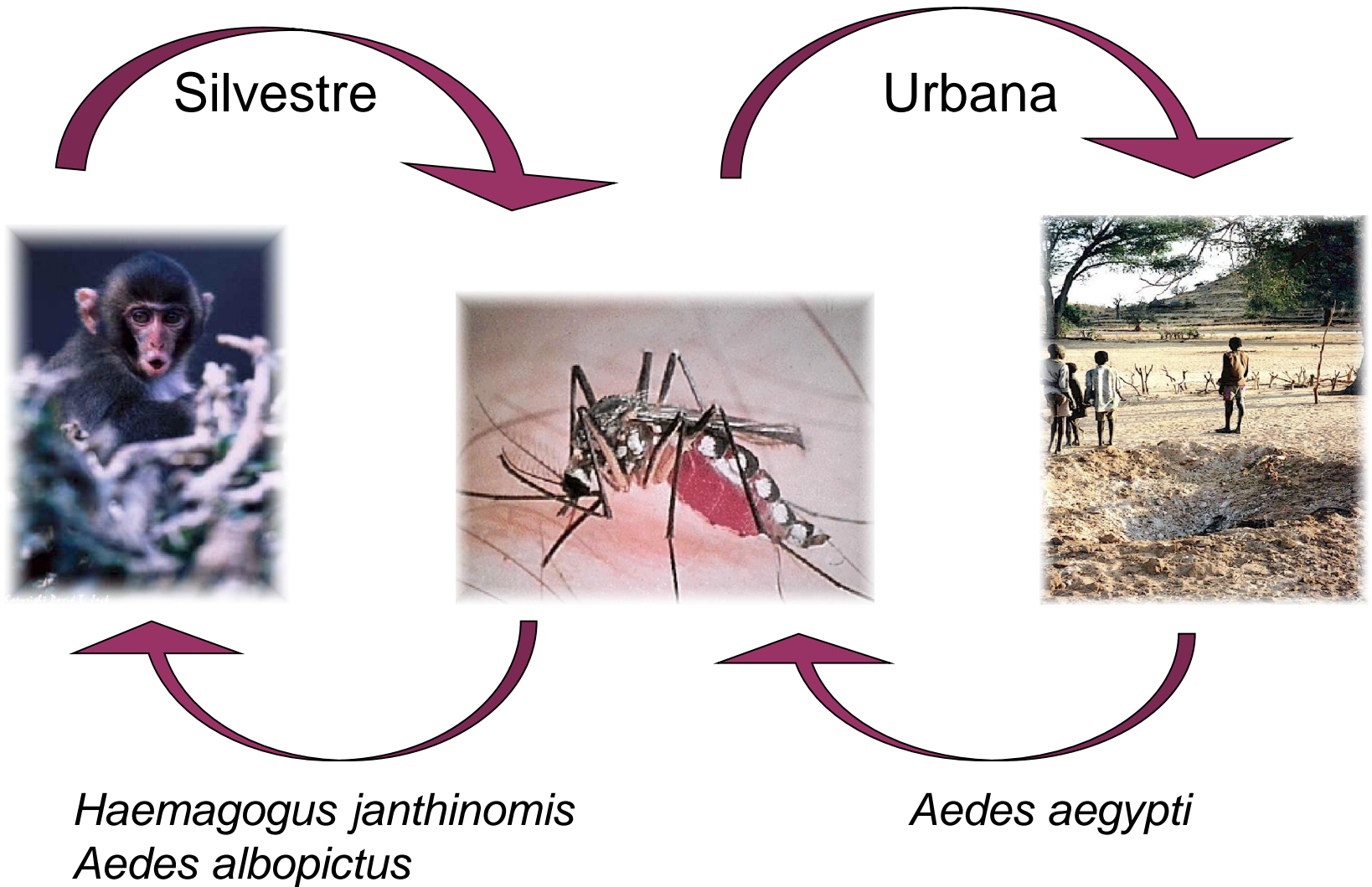


- 1- O mosquito infectado pica o hospedeiro e libera o vírus pela saliva.
- 2- O vírus replica-se nos órgãos alvos do hospedeiro.
- 3- O vírus infecta os linfócitos e tecidos linfáticos.
- 4- O vírus é liberado na circulação sanguínea.

- 5- Um segundo mosquito pica o hospedeiro infectado.
- 6- O mosquito ingere o vírus com o sangue. O vírus multiplica-se no trato digestivo do mosquito.
- 7- O vírus passa para as glândulas salivares, replica-se e será liberado da próxima vez que o inseto se alimentar.

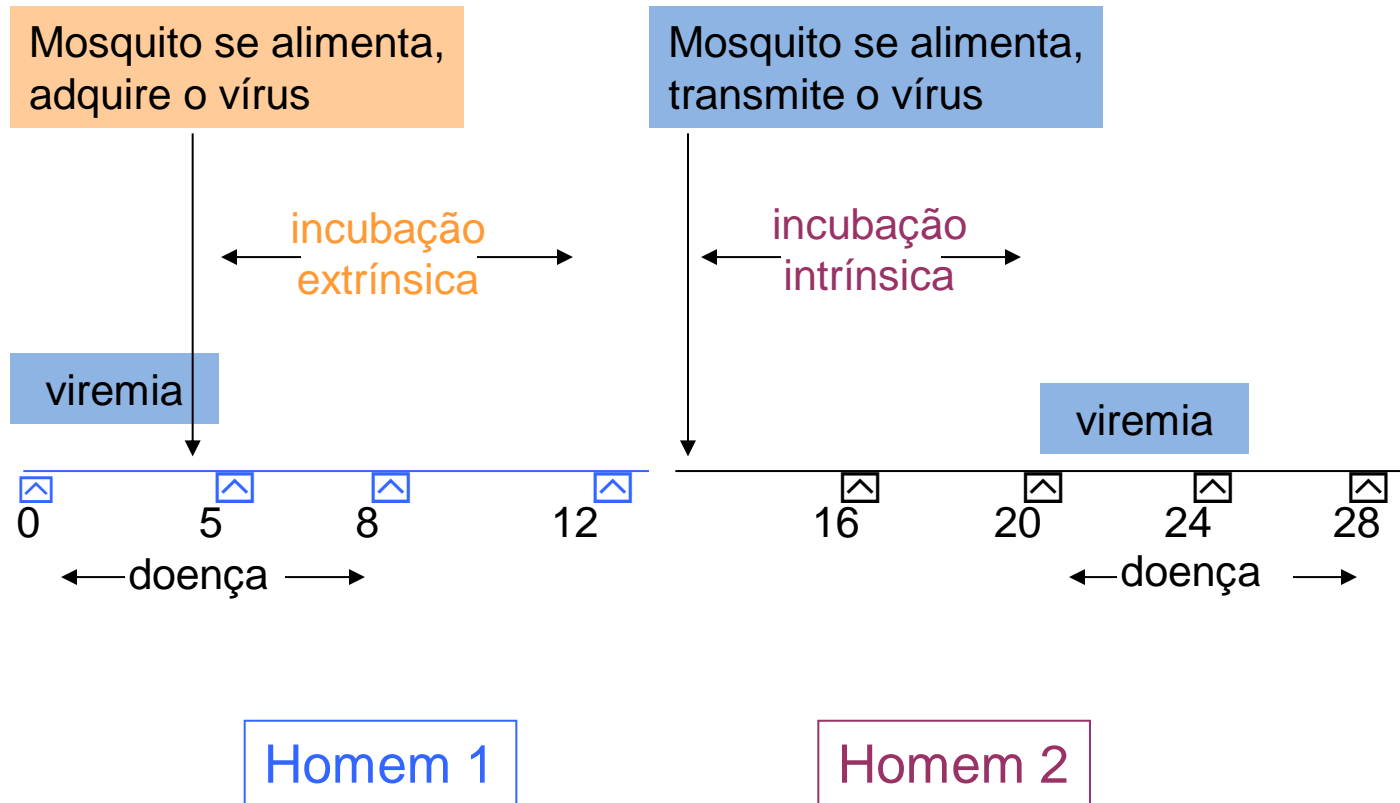
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Febre amarela



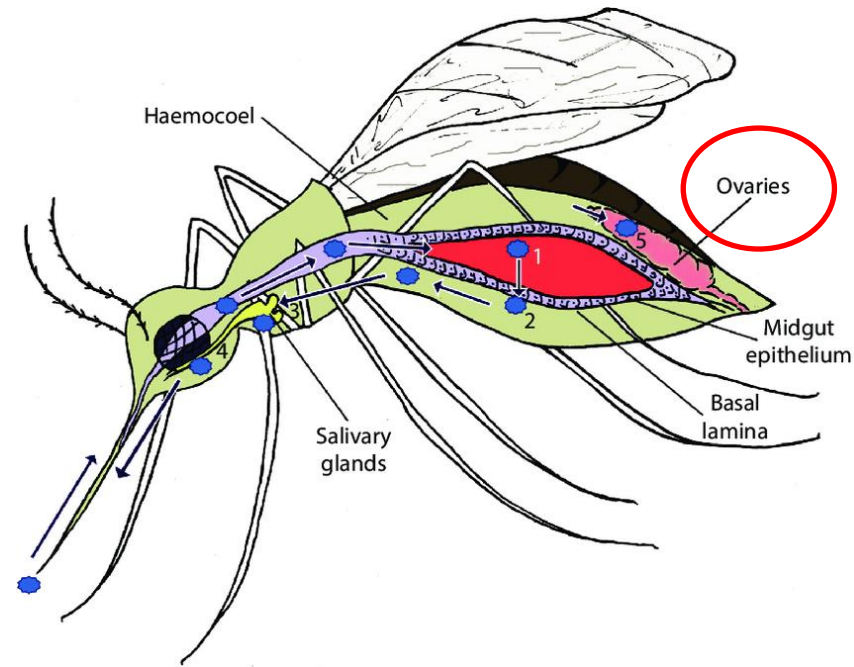
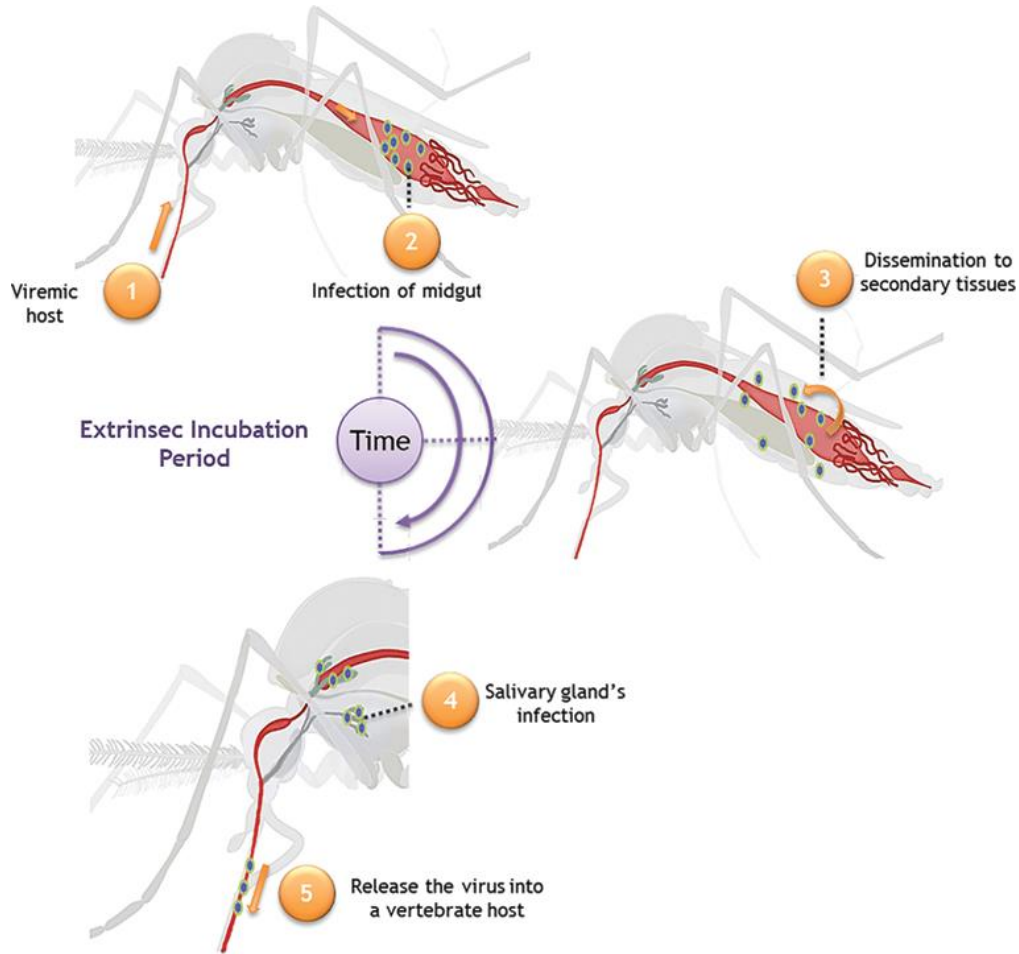
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Transmissão da dengue por *A. aegypti*



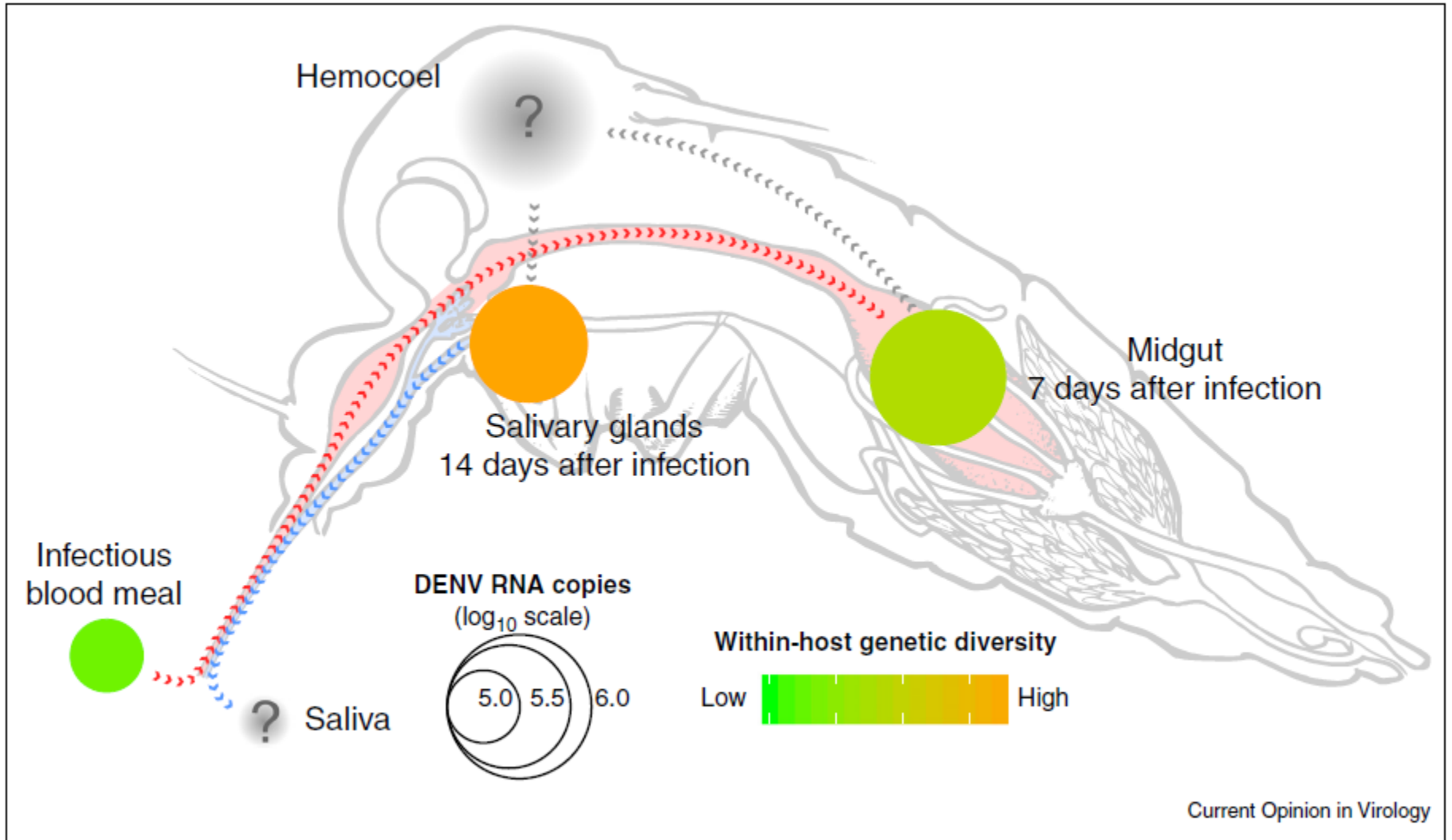
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Incubação extrínseca



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Incubação extrínseca



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Prevenção

- Controle do hospedeiro artrópode



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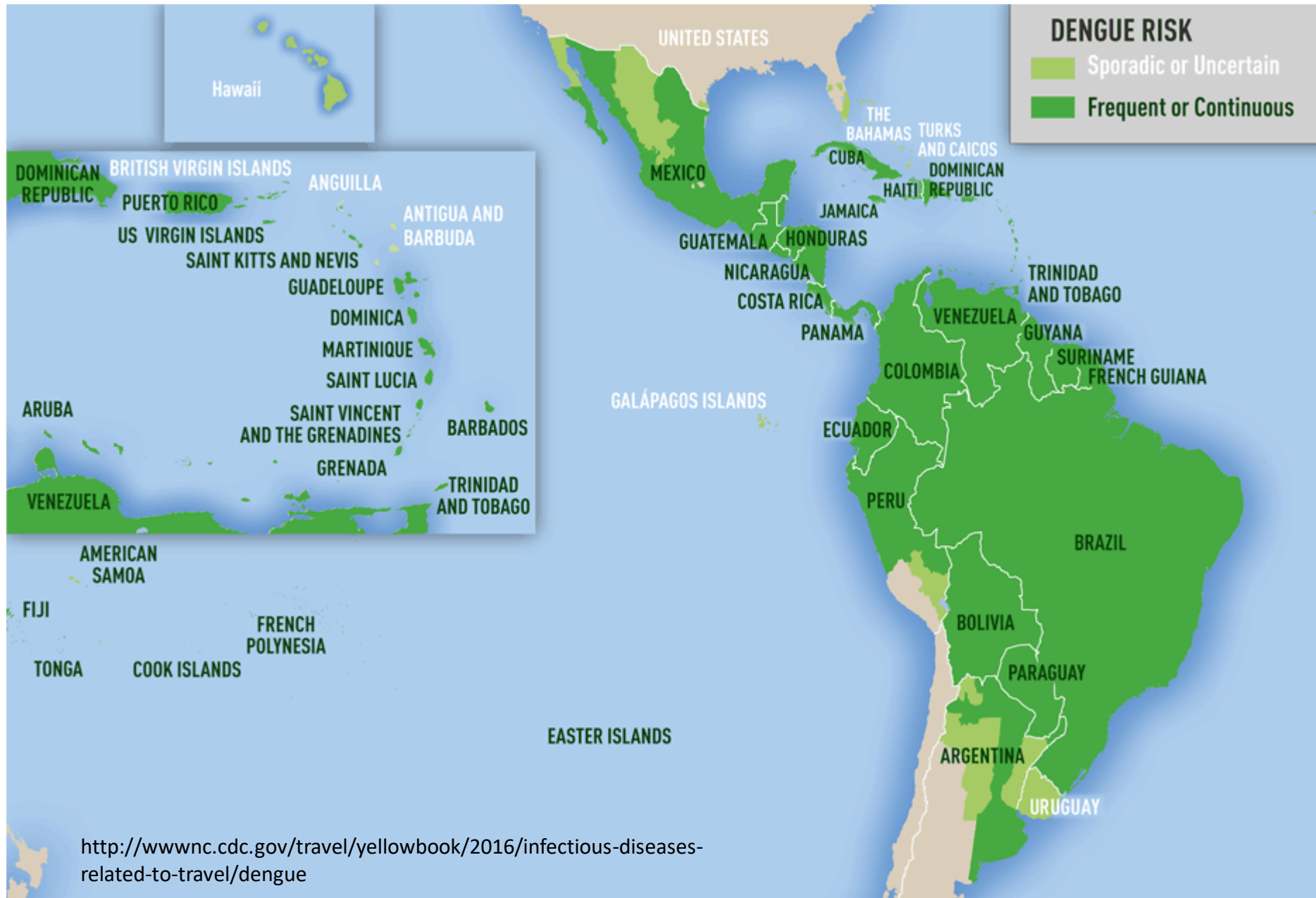
Prevenção



1970

Arboviroses

Prevenção



<http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/dengue>

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Prevenção

Febre Amarela

- Vacinação preventiva da população:
Vacina de vírus atenuados 17D

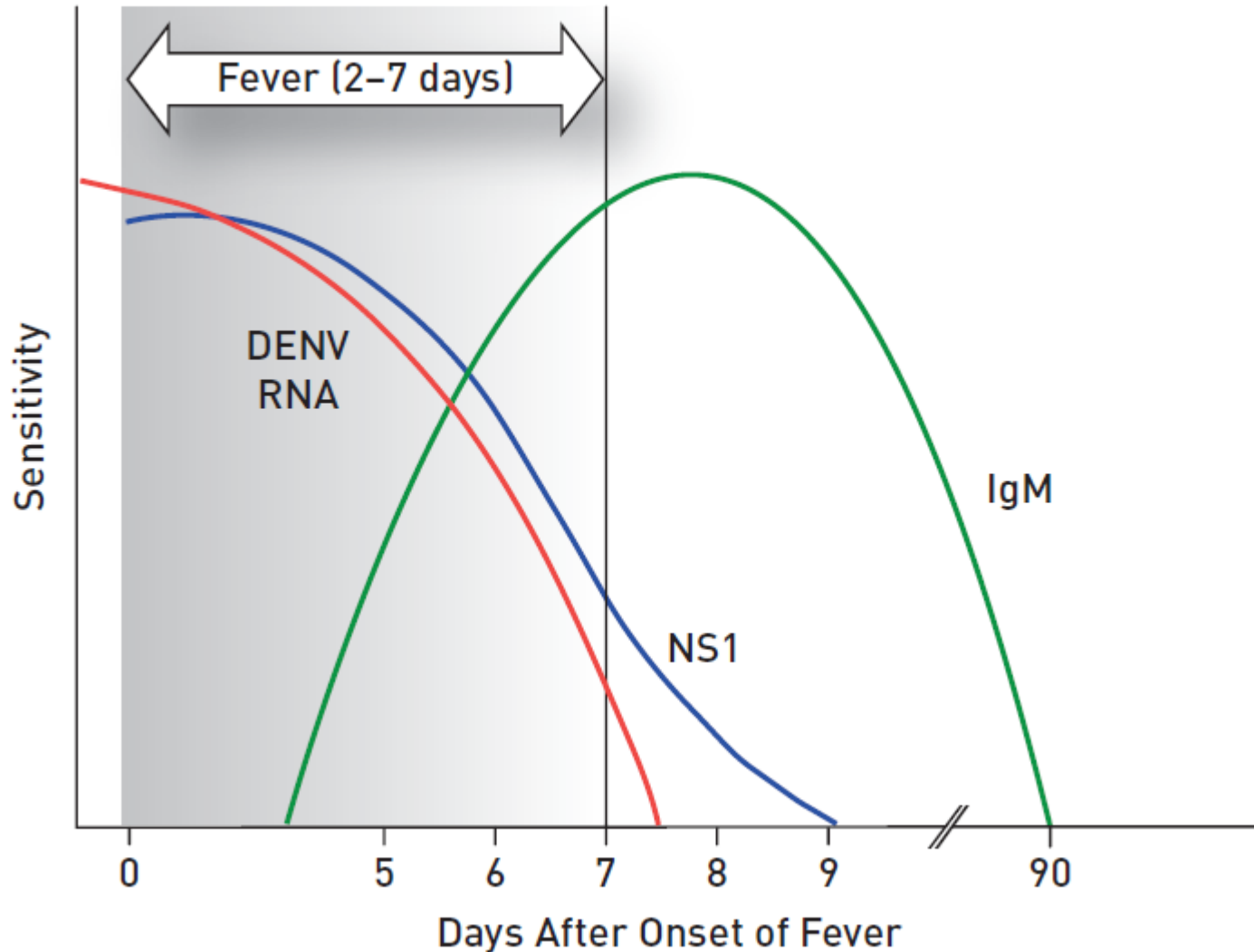
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Diagnóstico Laboratorial e Prevenção

- Diagnóstico Laboratorial
 - Isolamento viral em culturas de células de macaco (Vero ou LLC-MK2)
 - Soroneutralização
 - Imunofluorescência
 - Ensaio imunoenzimático (ELISA)
 - RT-PCR – hibridação
 - PCR

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Dengue: Diagnóstico Laboratorial



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Dengue: Diagnóstico Laboratorial

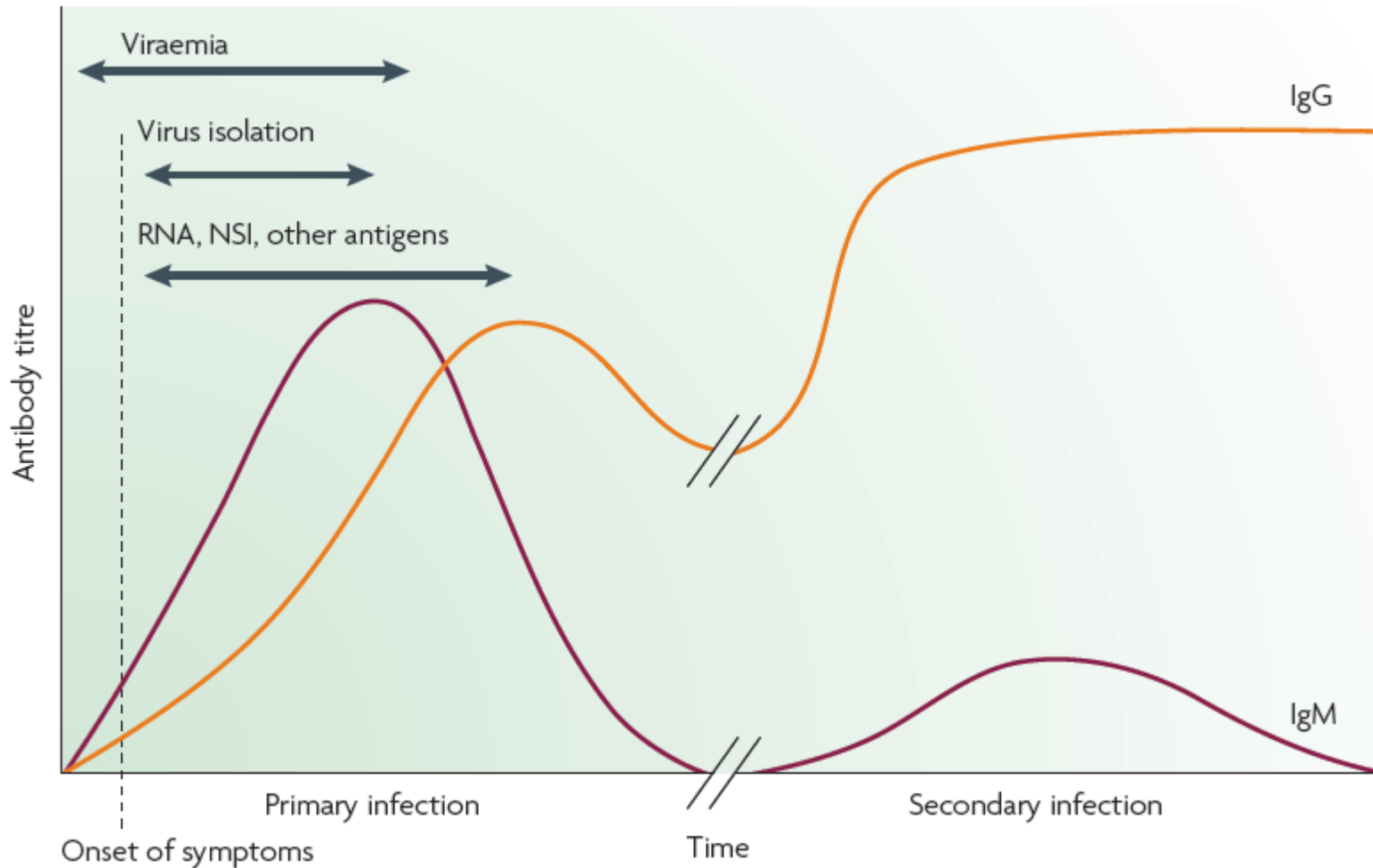


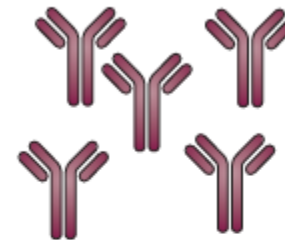
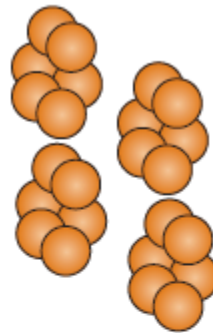
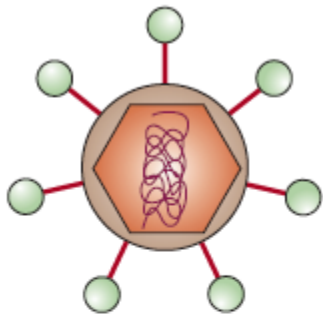
Figure 2 | **Major diagnostic markers for dengue infection.** The titre of the IgM and IgG response varies, depending on whether the infection is a primary or secondary infection.

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Dengue: Diagnóstico Laboratorial

Direct methods

Indirect methods



Virus
isolation

Genome
detection

Antigen
detection

Serology
IgM

Serology
IgG

Specificity

Opportunity

Figure 1 | **Comparative merits of direct and indirect laboratory methods for the diagnosis of dengue infections.** Opportunity refers to the fact that antibody testing is usually the most practical diagnostic option available.

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Dengue: Diagnóstico Laboratorial

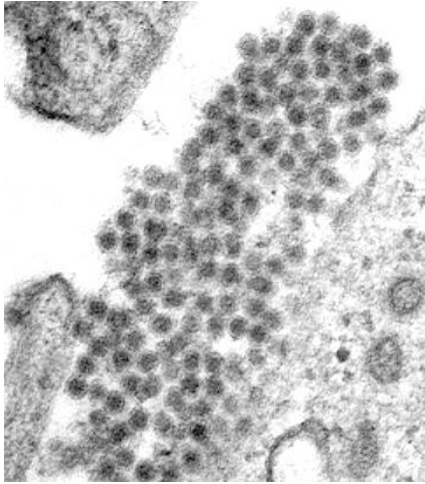
Table 1 | Advantages and limitations of different dengue diagnostic tests

Diagnostic tests	Advantages	Limitations
Viral isolation and identification	<ul style="list-style-type: none"> • Confirmed infection • Specific • Identifies serotypes 	<ul style="list-style-type: none"> • Requires acute sample (0–5 days post onset) • Requires expertise and appropriate facilities • Takes more than 1 week • Does not differentiate between primary and secondary infection • Expensive
RNA detection	<ul style="list-style-type: none"> • Confirmed infection • Sensitive and specific • Identifies serotype and genotype • Results in 24–48 hours 	<ul style="list-style-type: none"> • Potential false-positives owing to contamination • Requires acute sample (0–5 days post onset) • Requires expertise and expensive laboratory equipment • Does not differentiate between primary and secondary infection
<i>Antigen detection</i>		
Clinical specimens (for example, using blood in an NS1 assay)	<ul style="list-style-type: none"> • Confirmed infection • Easy to perform • Less expensive than virus isolation or RNA detection 	<ul style="list-style-type: none"> • Not as sensitive as virus isolation or RNA detection
Tissues from fatal cases (for immunohistochemistry, for example)	<ul style="list-style-type: none"> • Confirmed infection 	<ul style="list-style-type: none"> • Not as sensitive as virus isolation or RNA detection • Requires expertise in pathology
<i>Serological tests</i>		
IgM or IgG seroconversion	<ul style="list-style-type: none"> • Confirmed infection • Least expensive • Easy to perform 	<ul style="list-style-type: none"> • IgM levels can be low in secondary infections • Confirmation requires two or more serum samples • Can differentiate between primary and secondary infection*
IgM detection (single sample)	<ul style="list-style-type: none"> • Identifies probable dengue cases • Useful for surveillance, tracking outbreaks and monitoring effectiveness of interventions 	<ul style="list-style-type: none"> • IgM levels can be low in secondary infections

*Primary infection: IgM-positive and IgG-negative (if samples are taken before day 8–10); secondary infection: IgG should be higher than 1,280 haemagglutination inhibition in convalescent serum.

ARBOVIROSES “EMERGENTES”

Arboviroses Emergentes



Zika Vírus

Família: *Flaviviridae*

Gênero: *Flavivirus*

Transmissão: vetor artrópode - *Aedes aegypti*

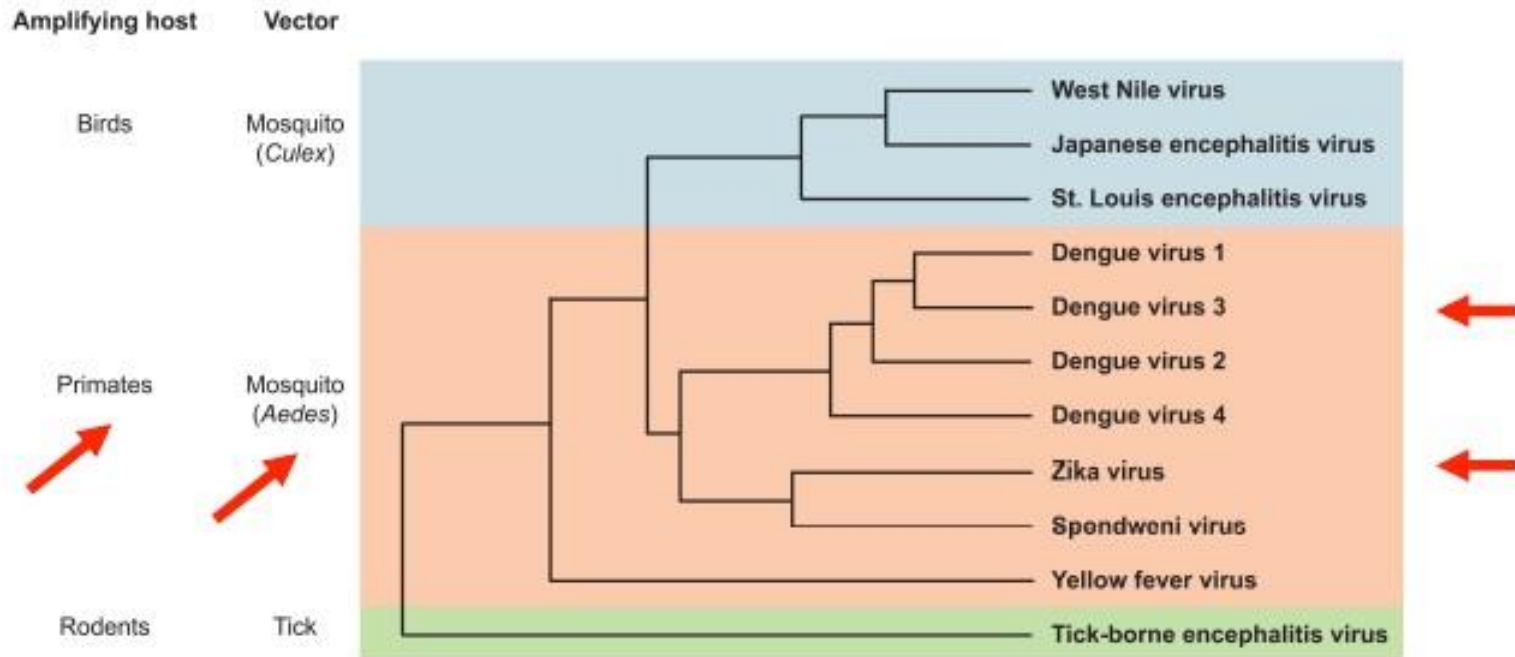
Partículas virais: esférico 45 nm, envelopado

Proteínas estruturais: glicoproteína E ; nucleoproteína: C; membrana: M

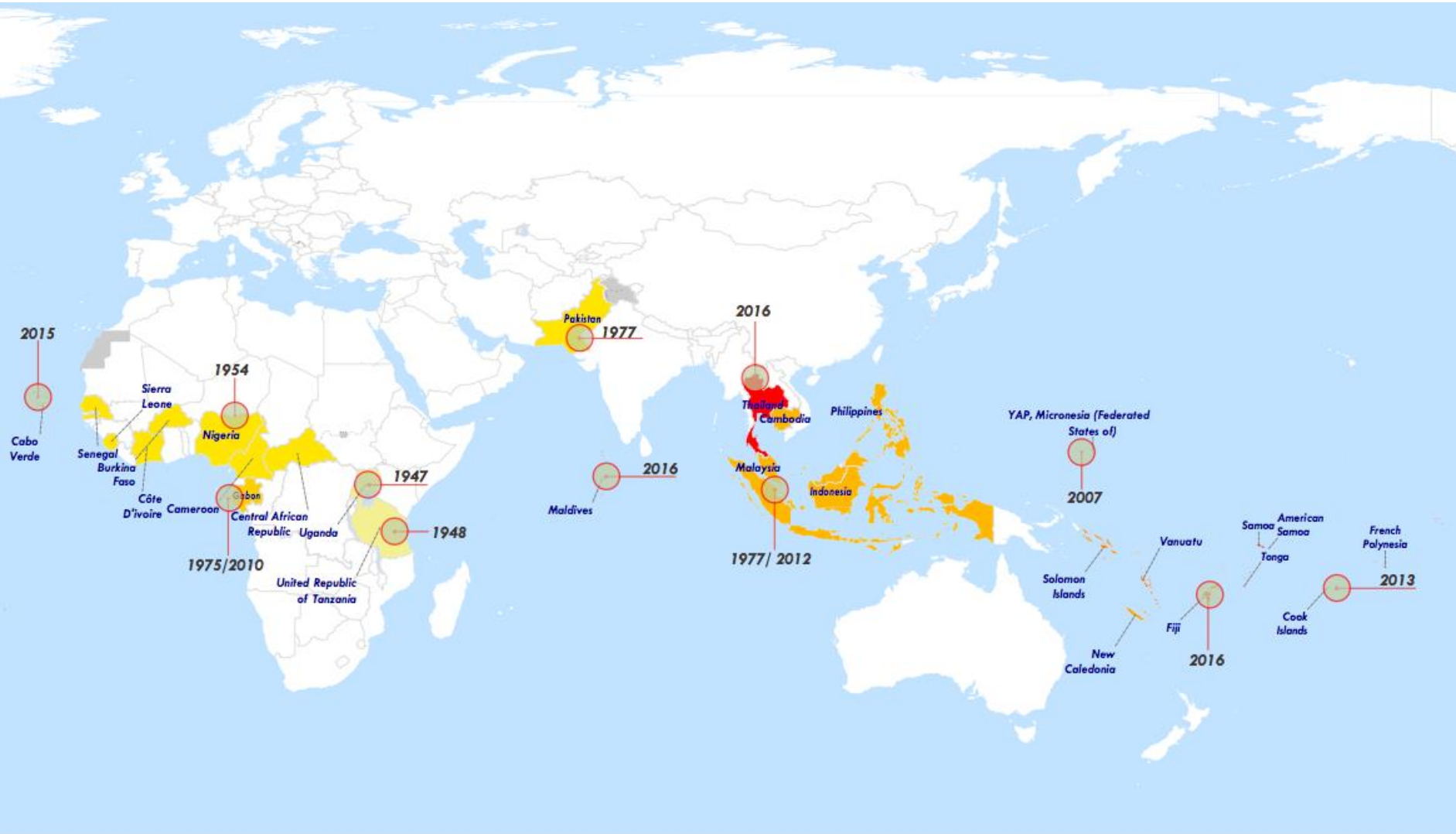
Genoma: ss-RNA polaridade positiva

Arboviroses Emergentes: Zika Vírus

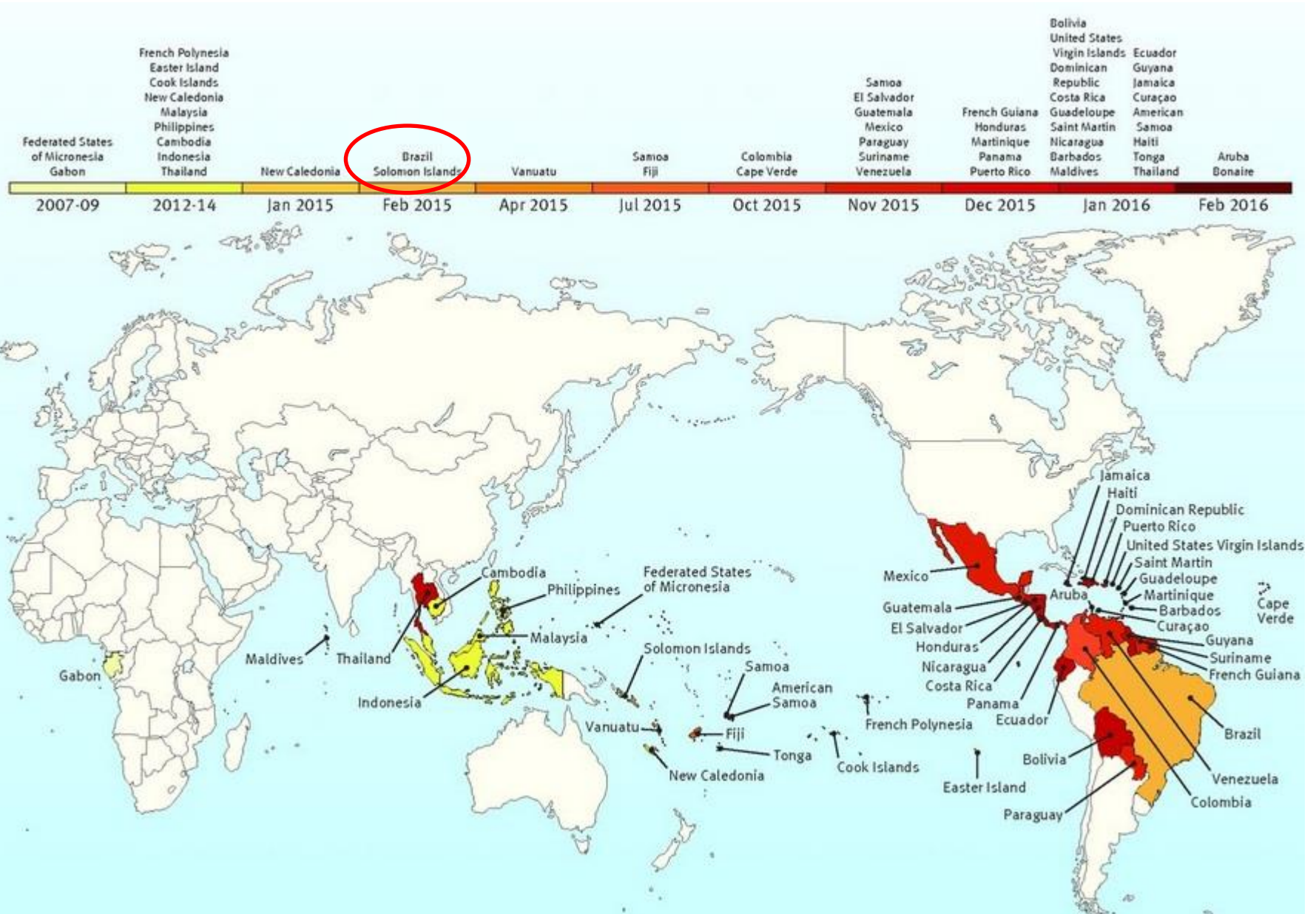
Zika virus is a flavivirus that is closely related to Dengue virus



Arboviroses Emergentes: Zika Vírus

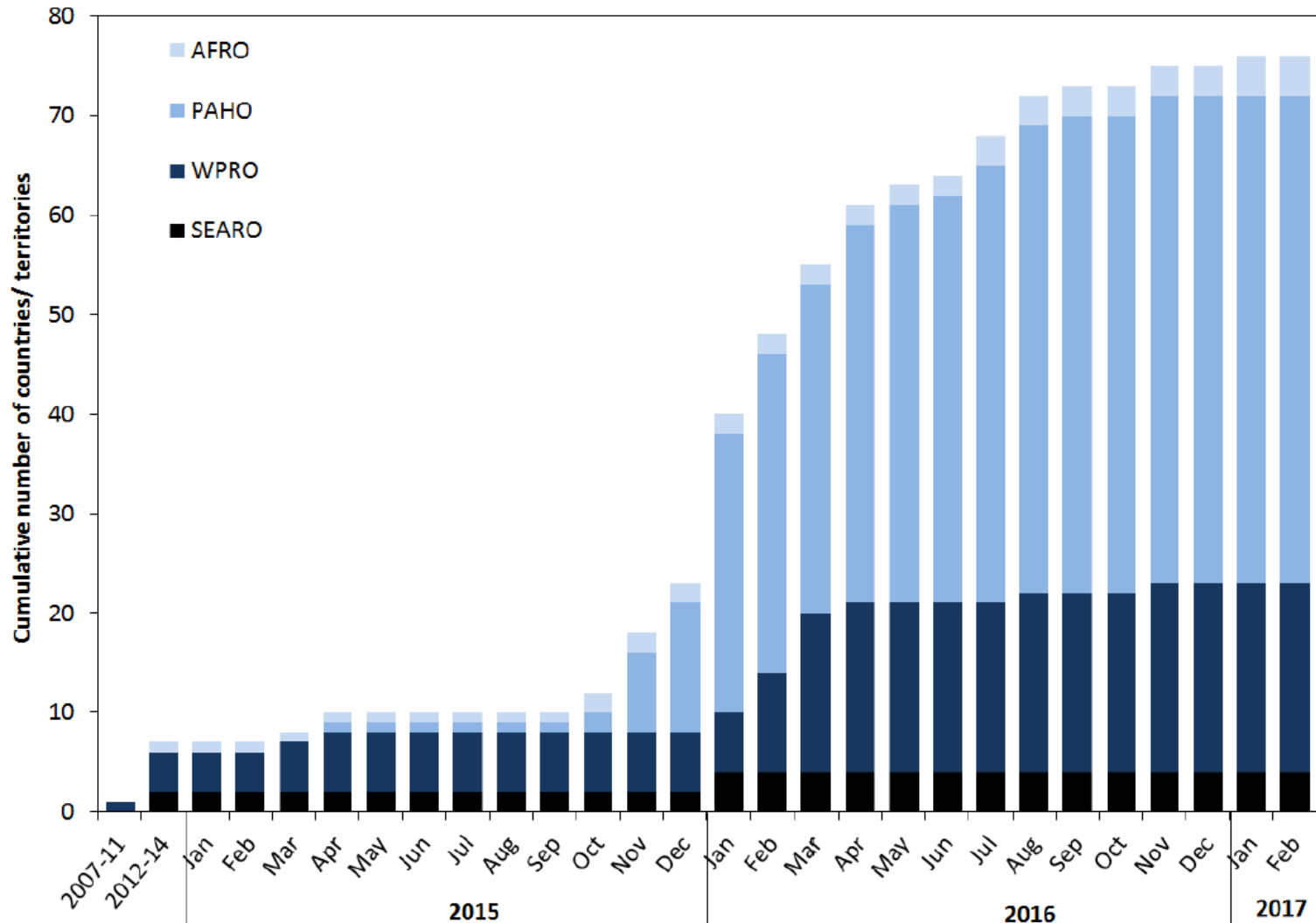


Arboviroses Emergentes: Zika Vírus



Arboviroses Emergentes: Zika Vírus

Figure 1. Cumulative number of countries and territories by WHO region¹ reporting mosquito-borne Zika virus transmission for the first time by year (2007–2014), and by month from 1 January 2015 to 1 February 2017



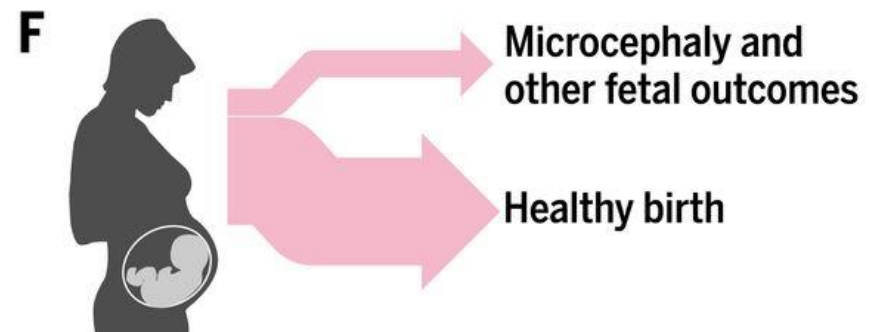
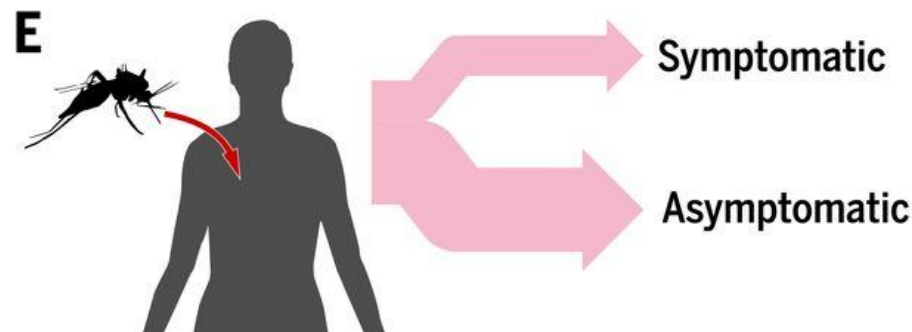
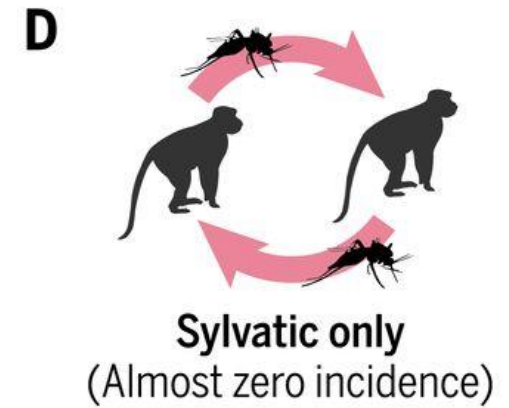
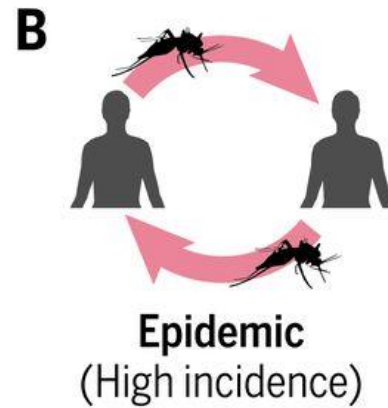
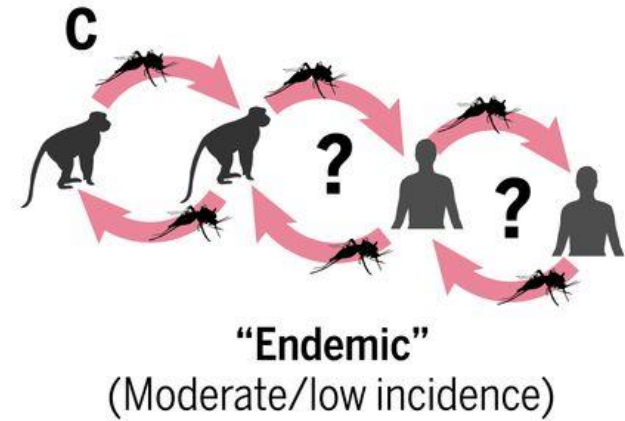
Arboviroses Emergentes: Zika Vírus

Figure 2. New detection of mosquito-borne Zika virus infections, January 2013–February 2017

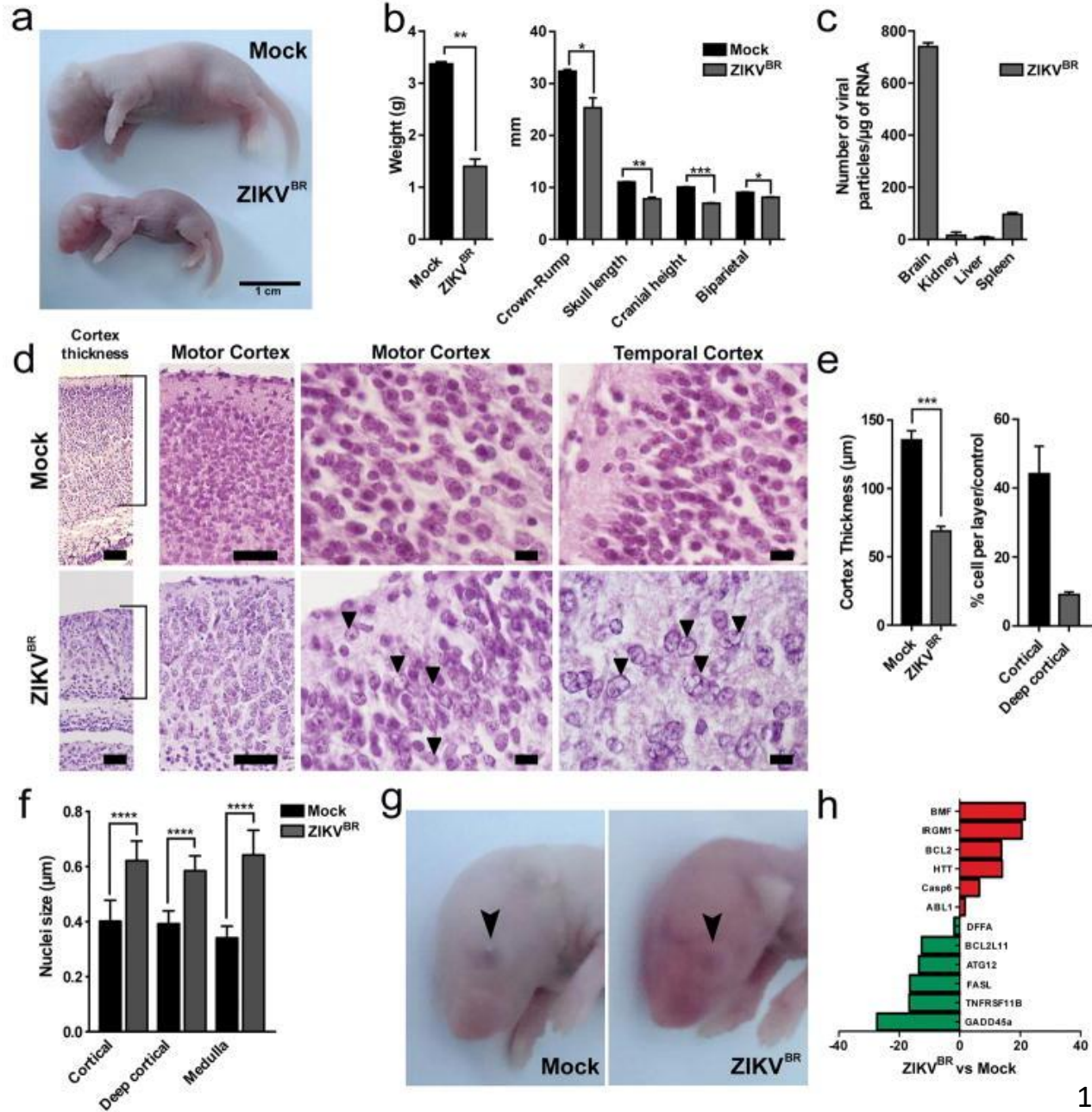


A report is considered an official notification from the government or a peer-reviewed publication. This map shows cases officially reported by the country/territory where infection occurred, and cases of returned travellers reported by countries other than the location of infection. Date of onset is used where known, otherwise date of report is used. Circulation of Zika virus in Indonesia, Malaysia, Philippines, Thailand and Viet Nam was reported before 2013, and Zika is considered to be possibly endemic in these countries. Countries where person-to-person transmission occurred are not represented in this map. Available information does not permit measurement of the risk of infection in any country; the variation in transmission intensity among countries is therefore NOT represented on this map. Zika virus is not necessarily present throughout the countries/territories shaded in this map.

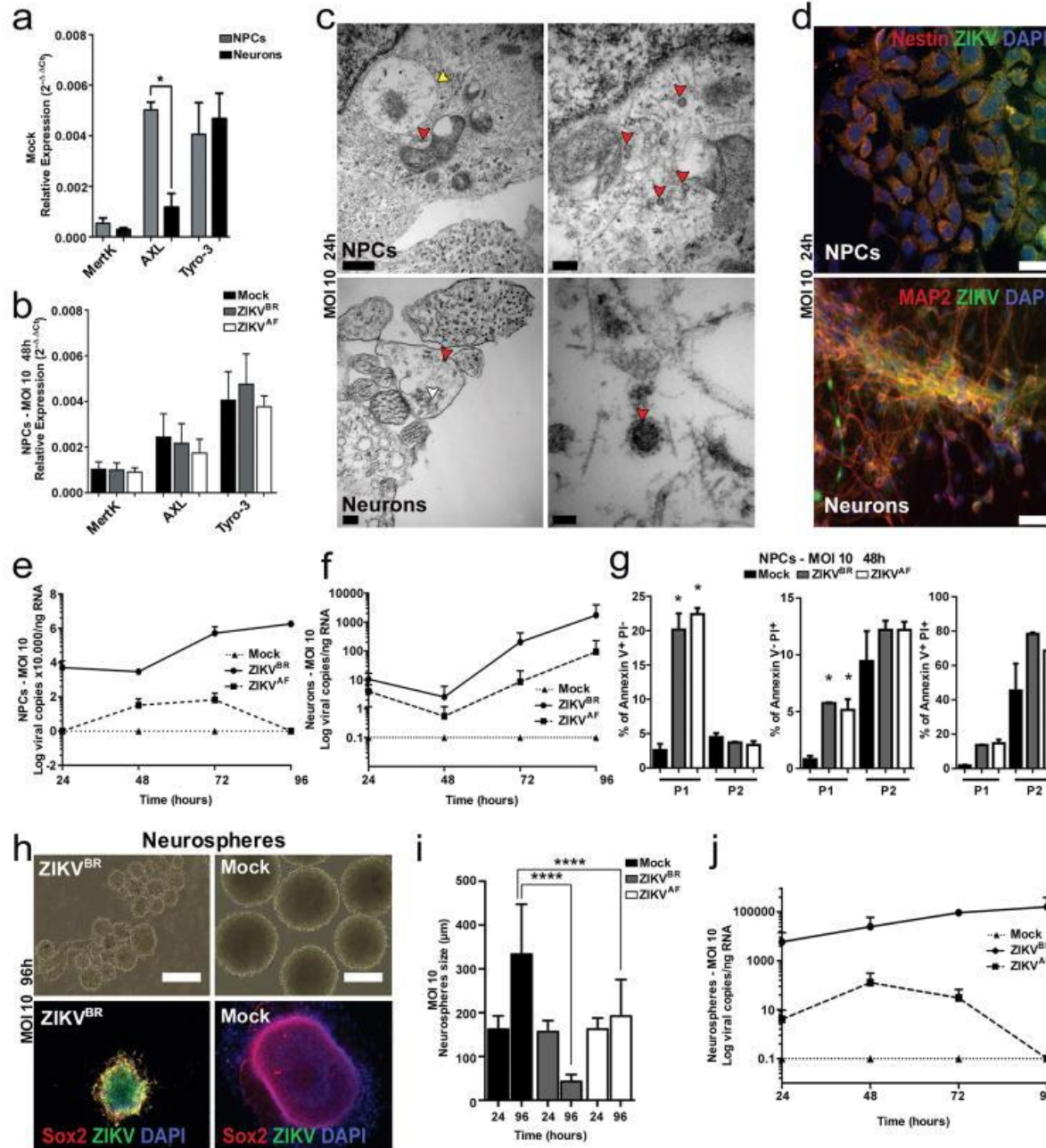
Arboviroses Emergentes: Zika Vírus



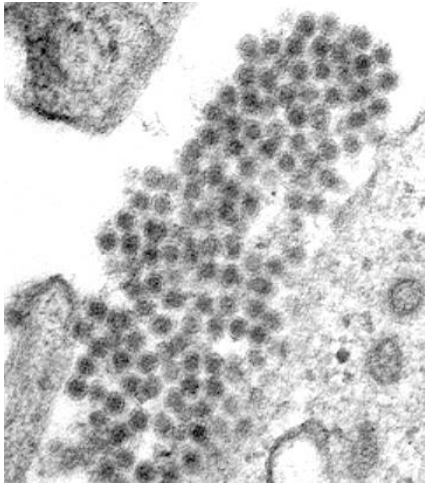
Arboviroses Emergentes: Zika Vírus



Arboviroses Emergentes: Zika Vírus



Arboviroses Emergentes



Chikungunya (Tanzania 1952)

Mayaro (Trinidad in 1954) (Genótipos D e L)

(Ross River virus, O'nyong'nyong virus, and Semliki Forest Virus (SFV))

Família: *Togaviridae*

Gênero: *Alphavirus*

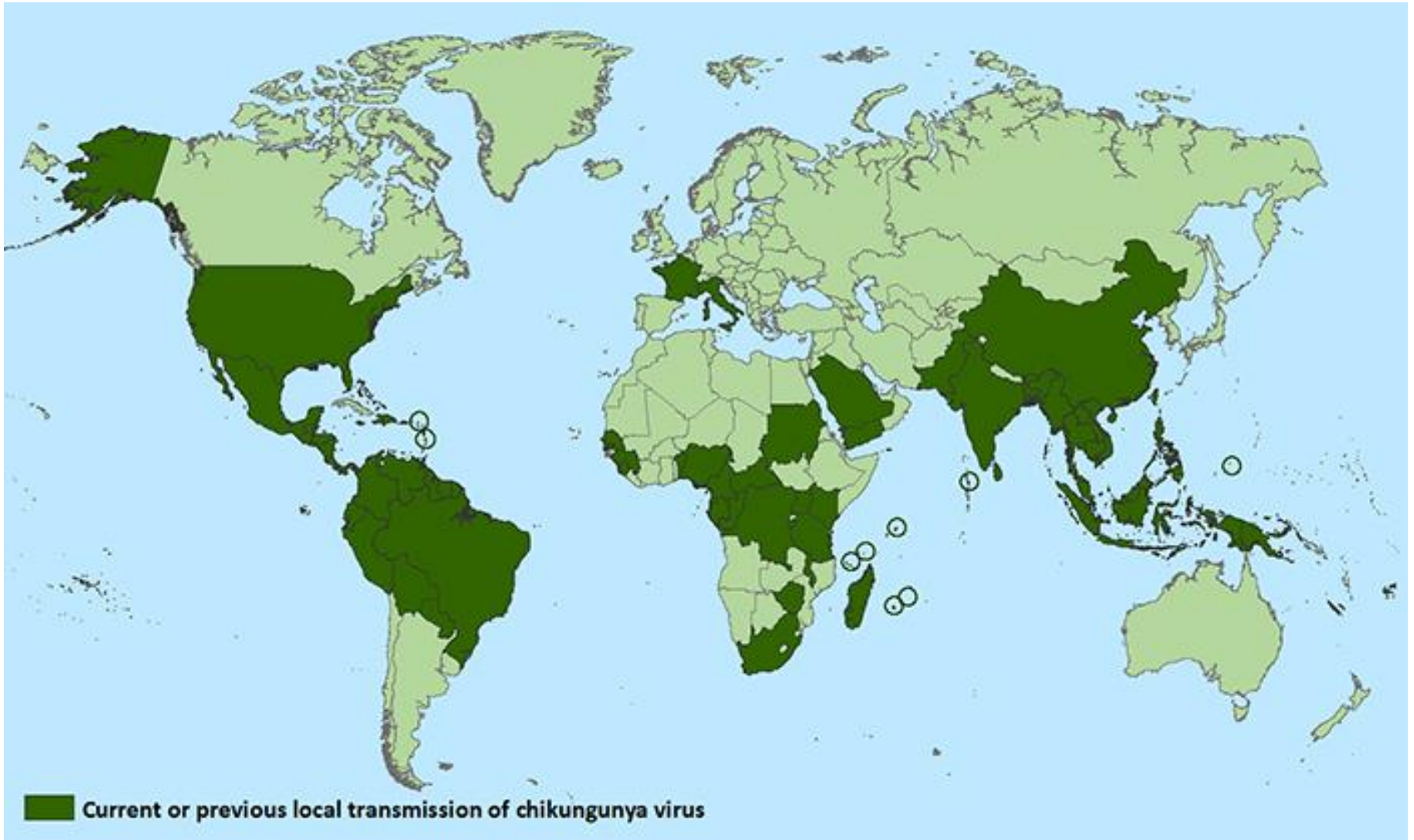
Transmissão: vetor artrópode - *Aedes aegypti* ((*Ae. furcifer*, *Ae. taylori* e *Ae. luteocephalus*)

Partículas virais: esférico 60-70 nm, envelopado

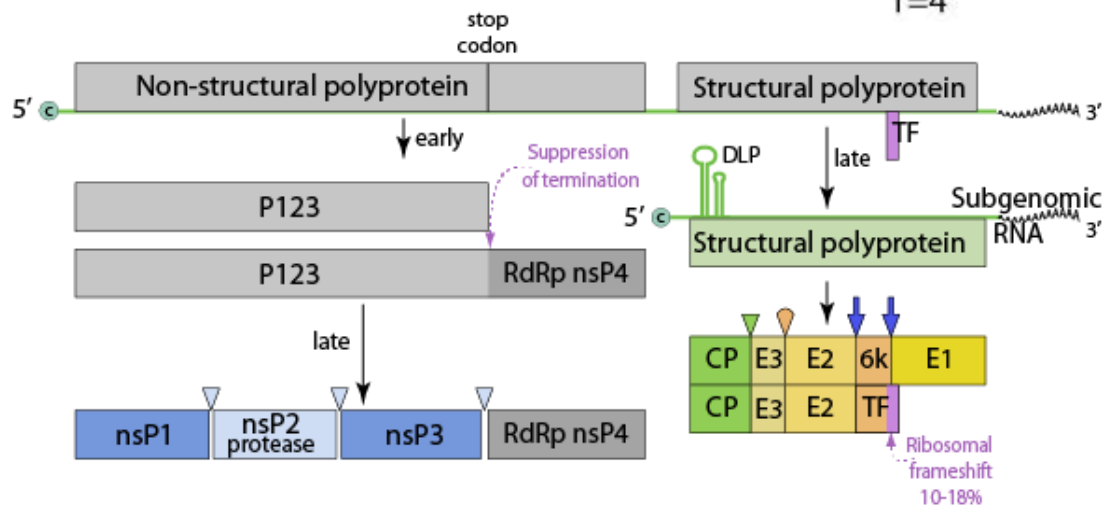
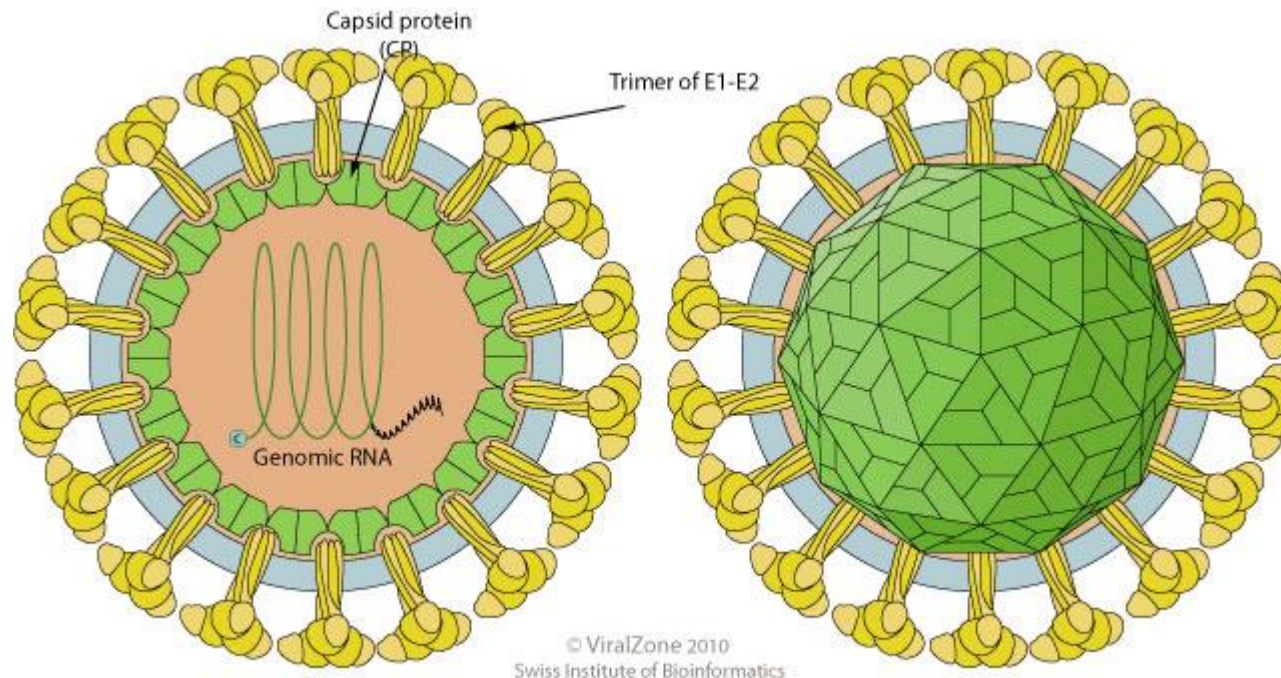
Proteínas estruturais: E2, E3, CP, 6k e TF

Genoma: ss-RNA polaridade positiva 11.6 kb

Arboviroses Emergentes: Chikungunya



Arboviroses Emergentes: Chikungunya



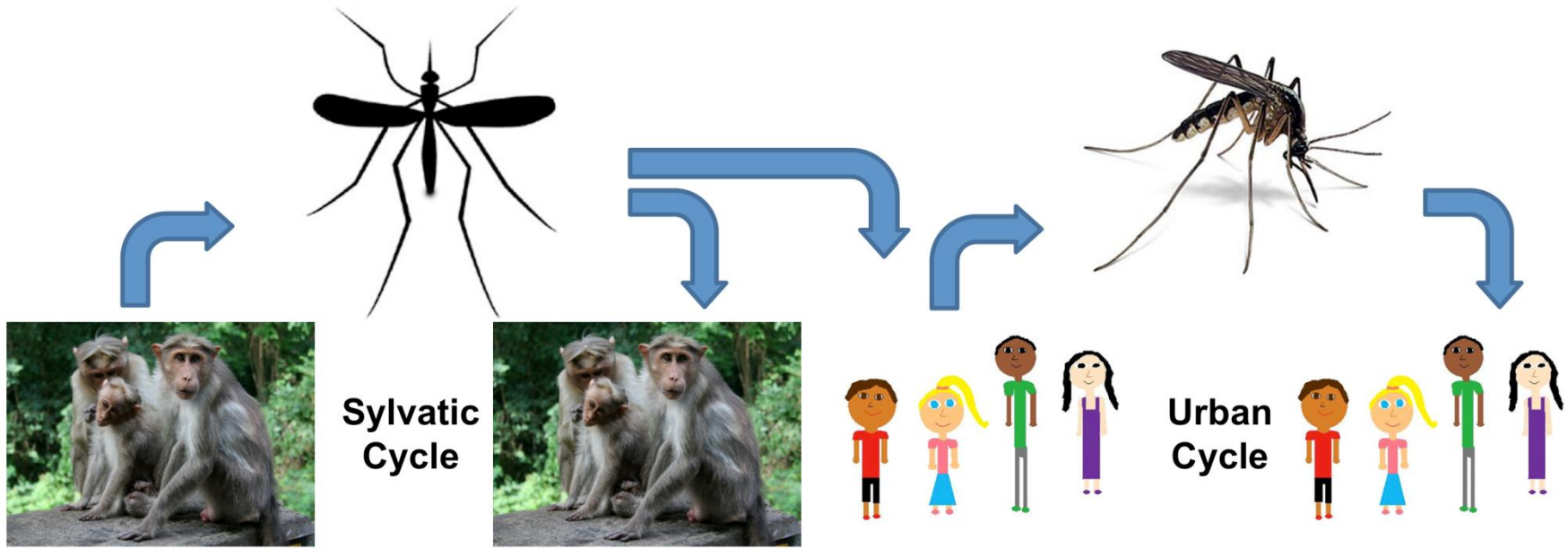
▽ by nsP2 protease

▽ by capsid

▽ by furin

↓ by signal peptidase

Arboviroses Emergentes: Chikungunya



Chimpanzees, monkeys, baboons



e.g. *Ae. africanus*
Ae. furcifer-taylori
Ae. dalzieli



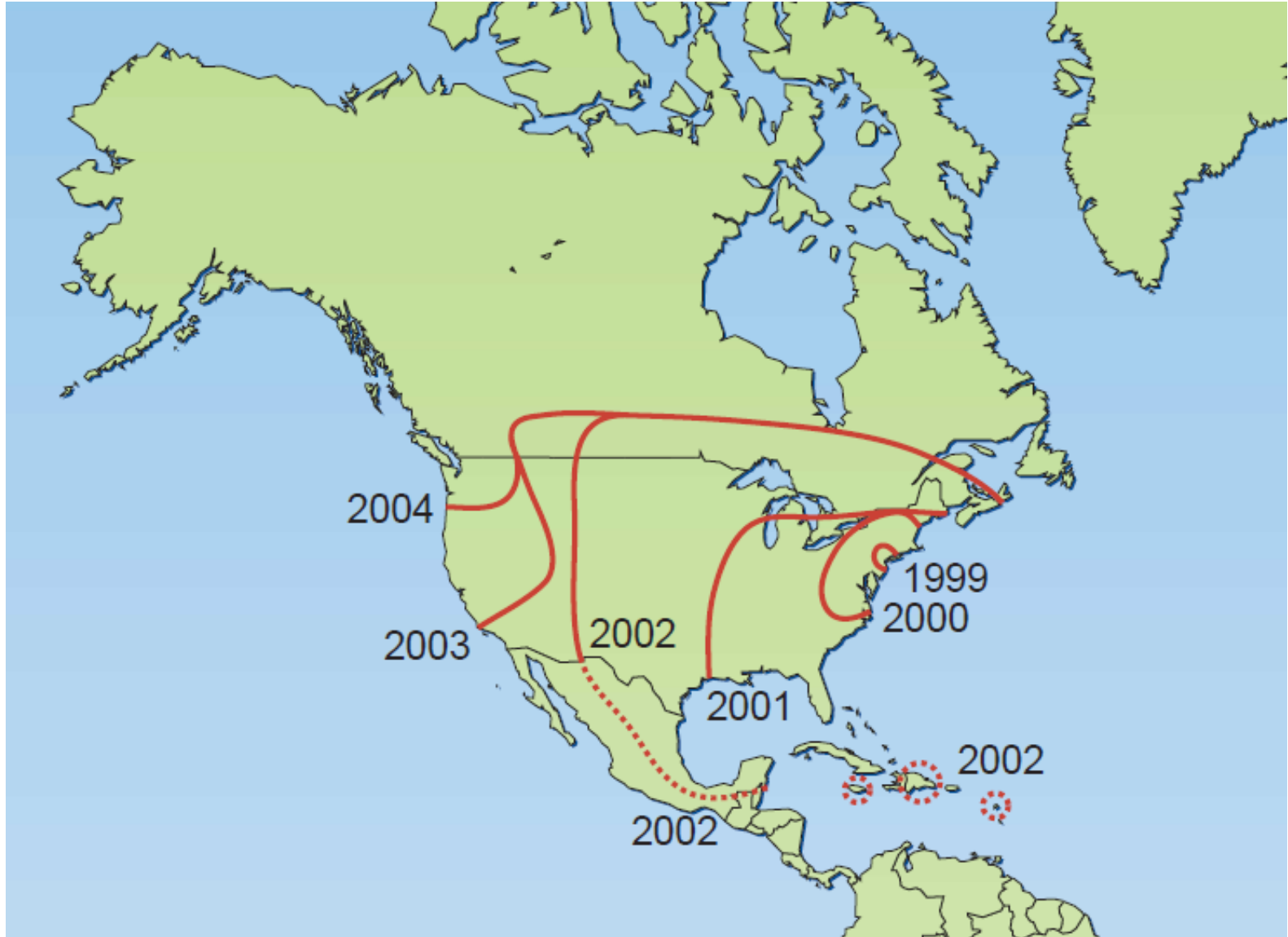
e.g. *Ae. aegypti*
Ae. albopictus

Arboviroses Emergentes...

É bom ficarmos atentos!!!

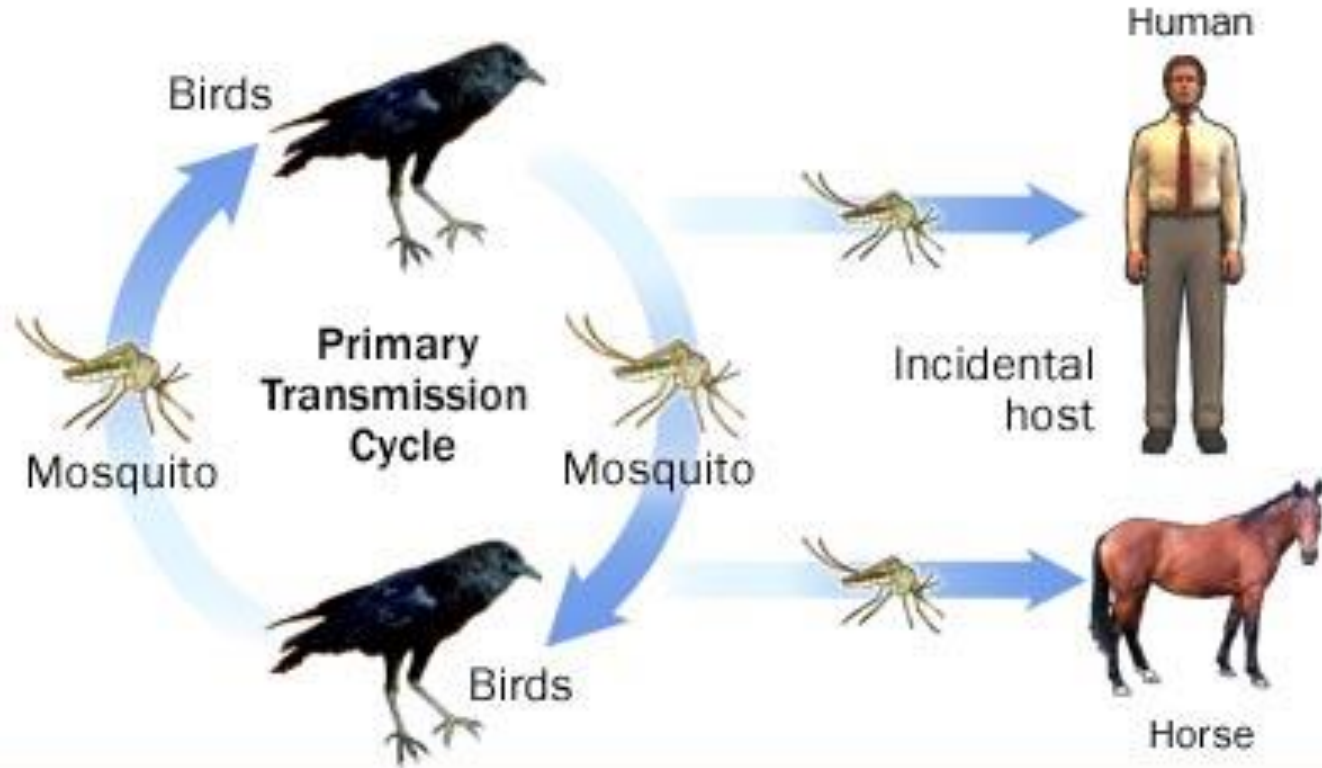
Arboviroses Emergentes: West Nile (flavivírus)

West Nile virus (WNV)



Arboviroses Emergentes: West Nile (flavivírus)

West Nile virus (WNV)

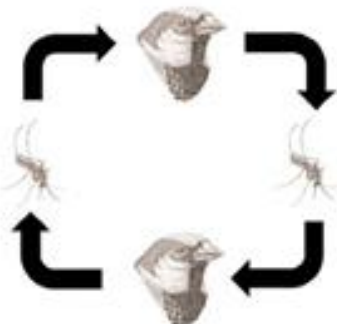
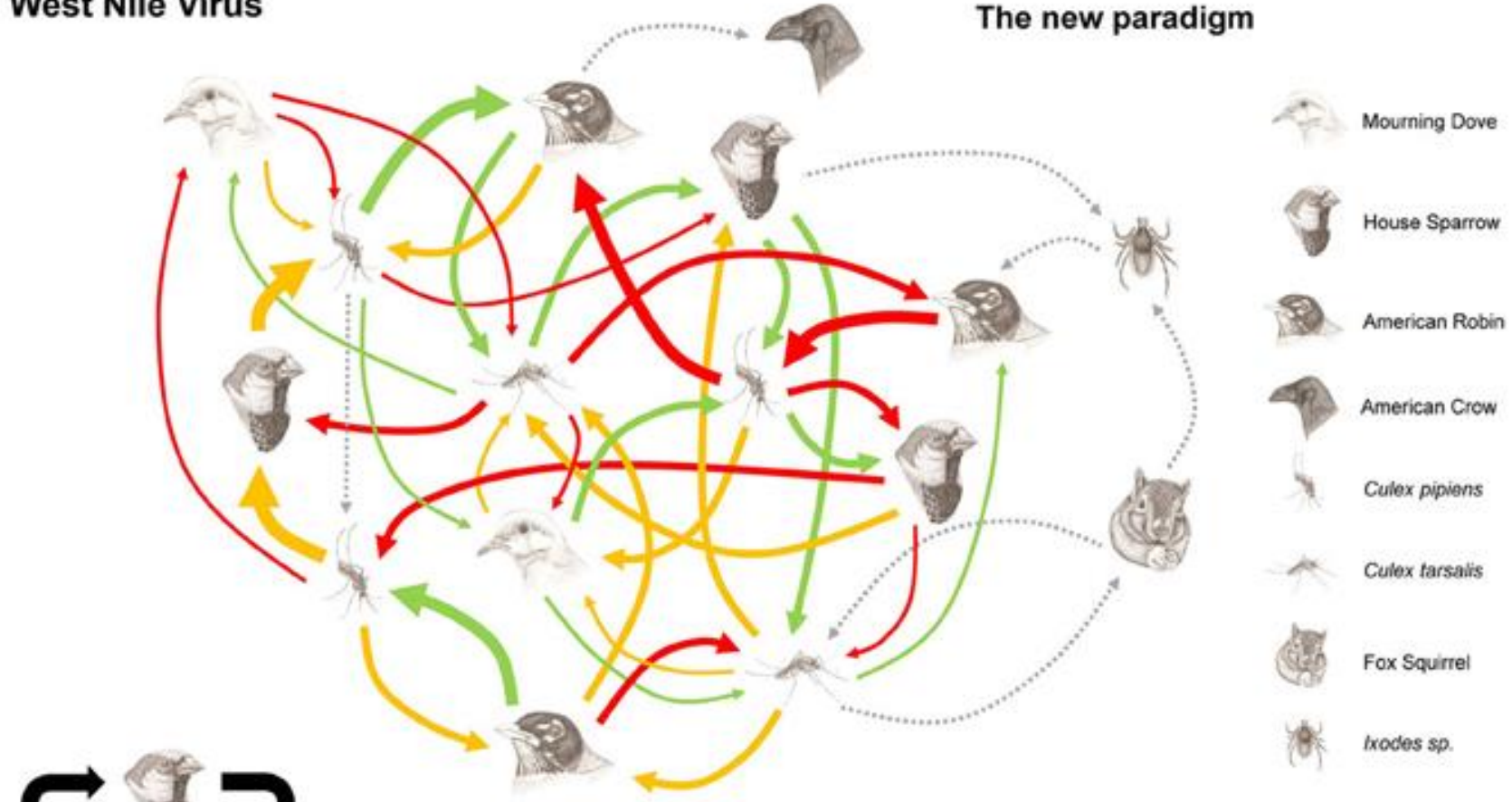


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Arboviroses: ciclos de transmissão mais complexos?

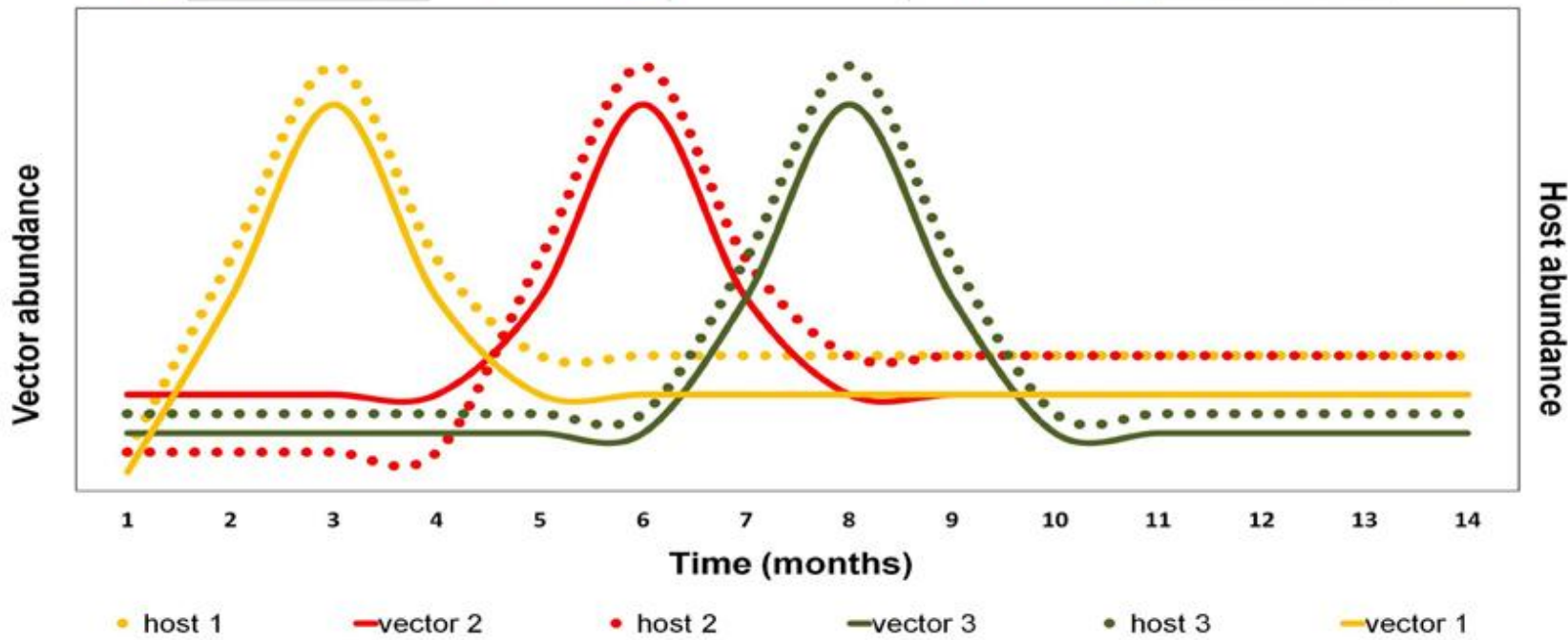
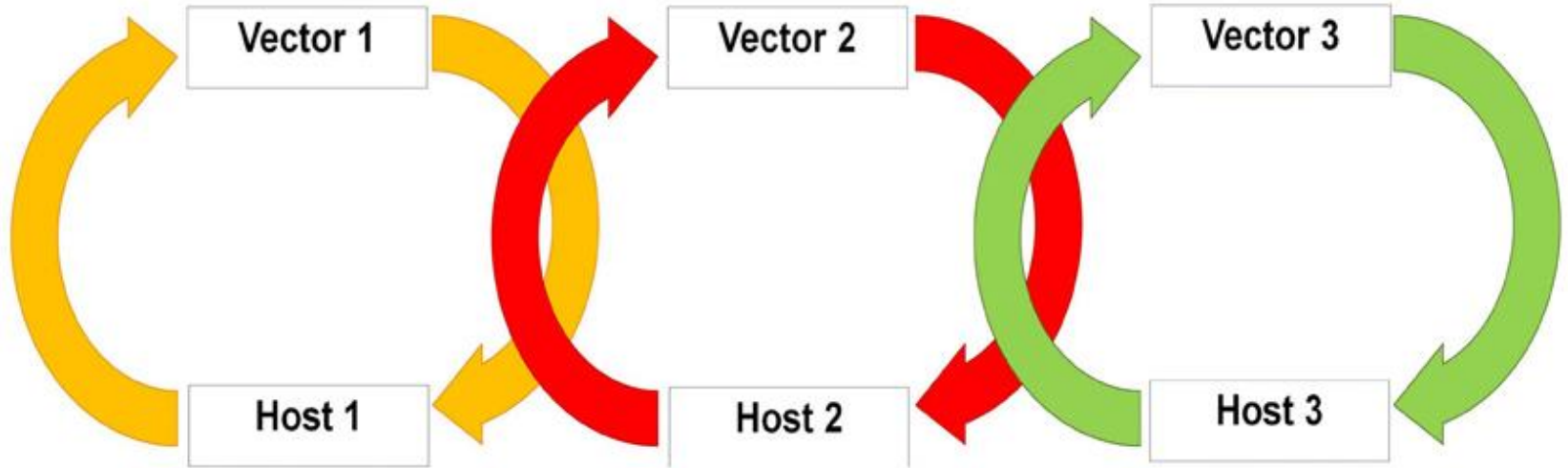
West Nile Virus

The new paradigm



The old paradigm

Arboviroses: ciclos de transmissão mais complexos?



Outras Arboviroses: Oropouche



Família: *Bunyaviridae* (Gênero *Orthobunyavirus*)

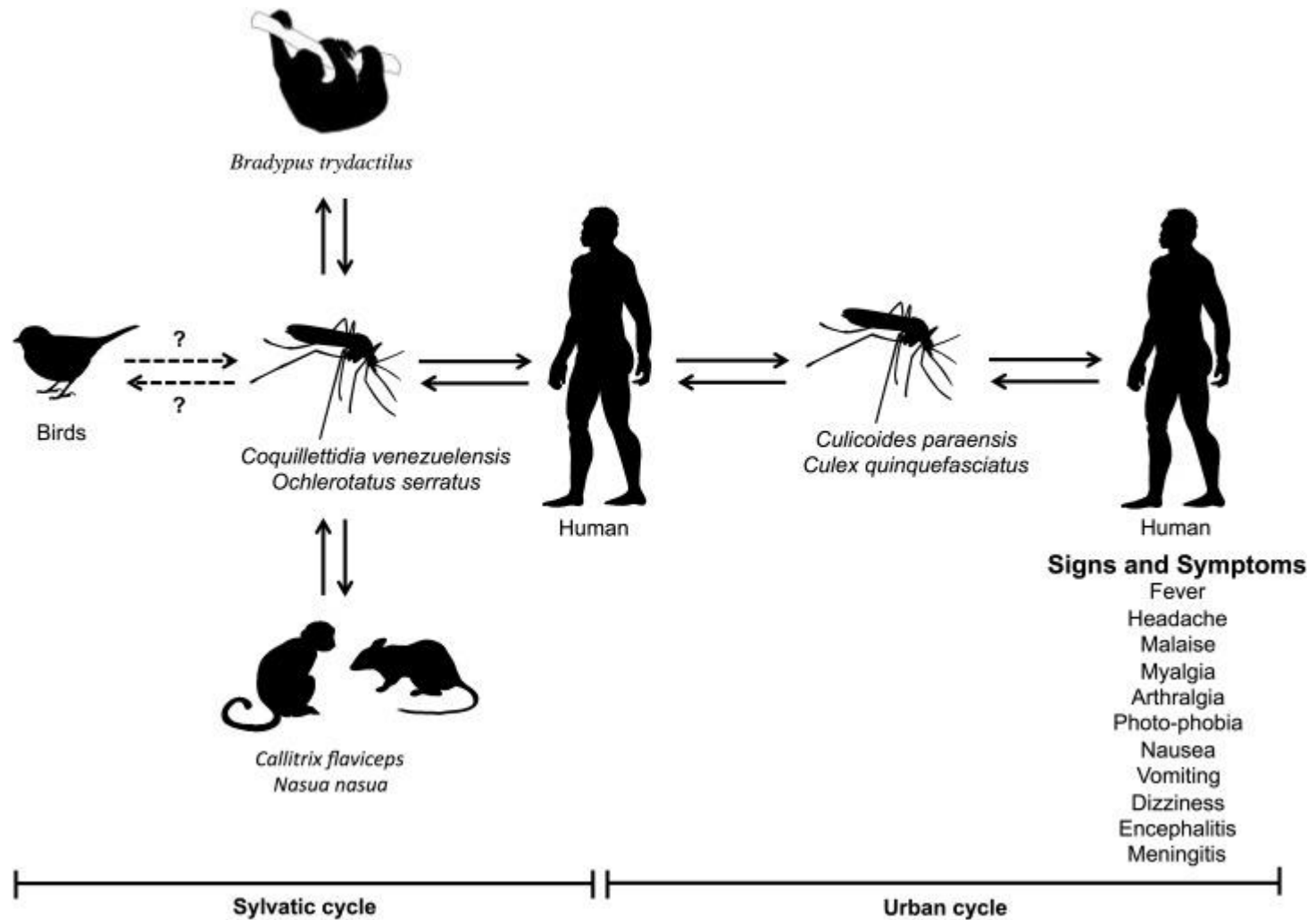
Transmissão: hospedeiro vertebrado, sem vetor artrópode

Partículas virais: esférico, 80-110 nm

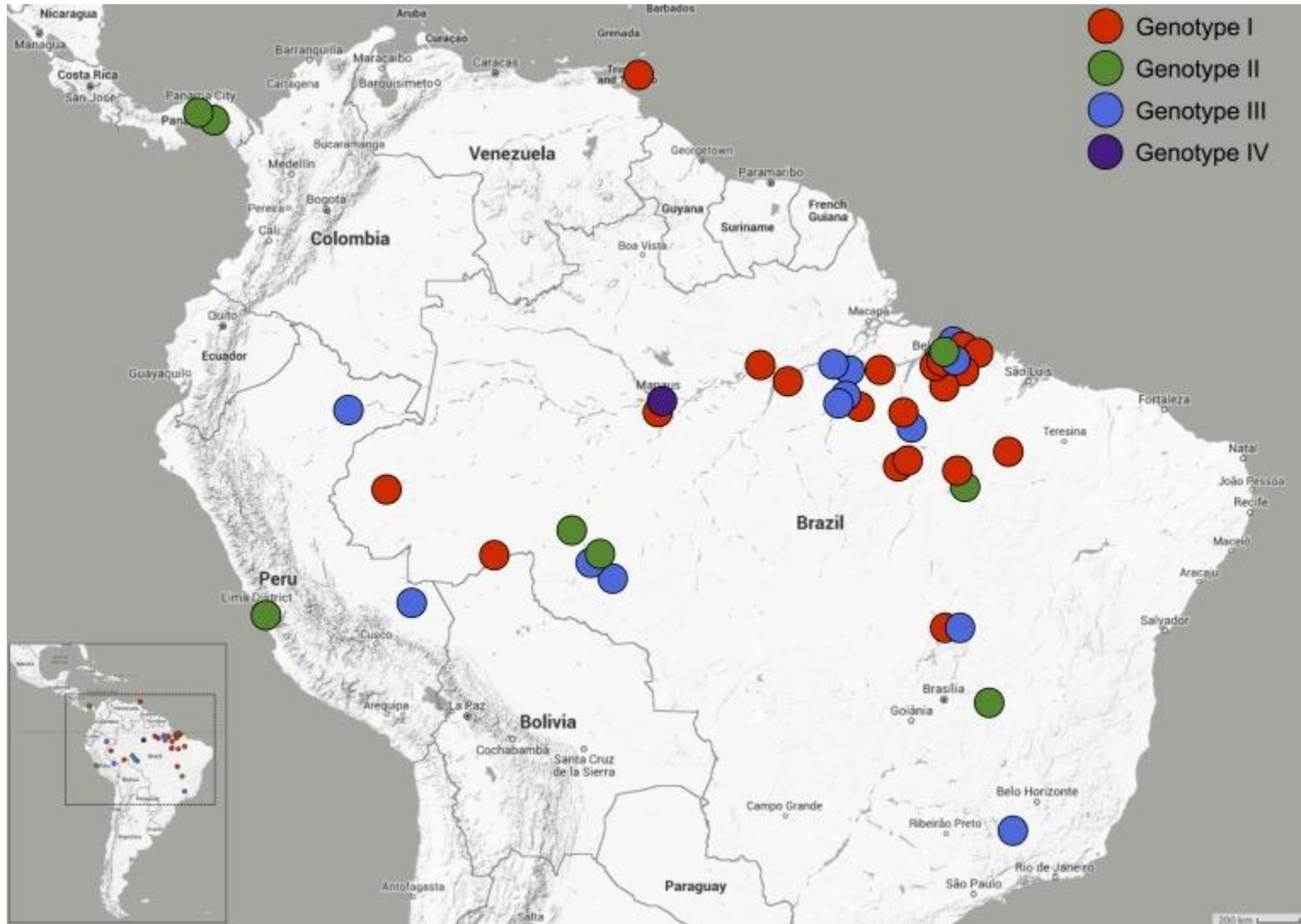
Proteínas estruturais: glicoproteínas: G1, G2 ; nucleoproteína: N

Genoma: ss-RNA, trisegmentado, polaridade negativa

Outras Arboviroses: Oropouche



Outras Arboviroses: Oropouche



VÍRUS EMERGENTES

Alterações nas populações de hospedeiros e no meio ambiente podem expandir os nichos para disseminação viral:

Exemplos:

- Poliomielite e saneamento básico
- Varíola e Sarampo no novo mundo
- Hantavírus e mudanças climáticas (Sin nombre vírus, 1993)
- Aedes...
- Barragens...

OBRIGADO!!!