BIOS27816: Population biology of infectious diseases of global health concern

Transmission dynamics and interventions for Vector-Borne Diseases

UChicago Center in Paris

Paris, France

January 2024

Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

- **Vector-borne** diseases (a type of indirect transmission) are transmitted via blood-feeding arthropod (mosquitoes, ticks, fleas)
  - Euclidean **vector**: a quantity with a magnitude and direction

  - Epidemiological **vector**: an agent that carries and transmits an infectious patient into another living organism

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  - Sleeping sickness, also known as African trypanosomiasis: tsetse fly vector and protozoan pathogen (trypanosome)
  - Chagas disease: kissing bug vector and trypanosome pathogen
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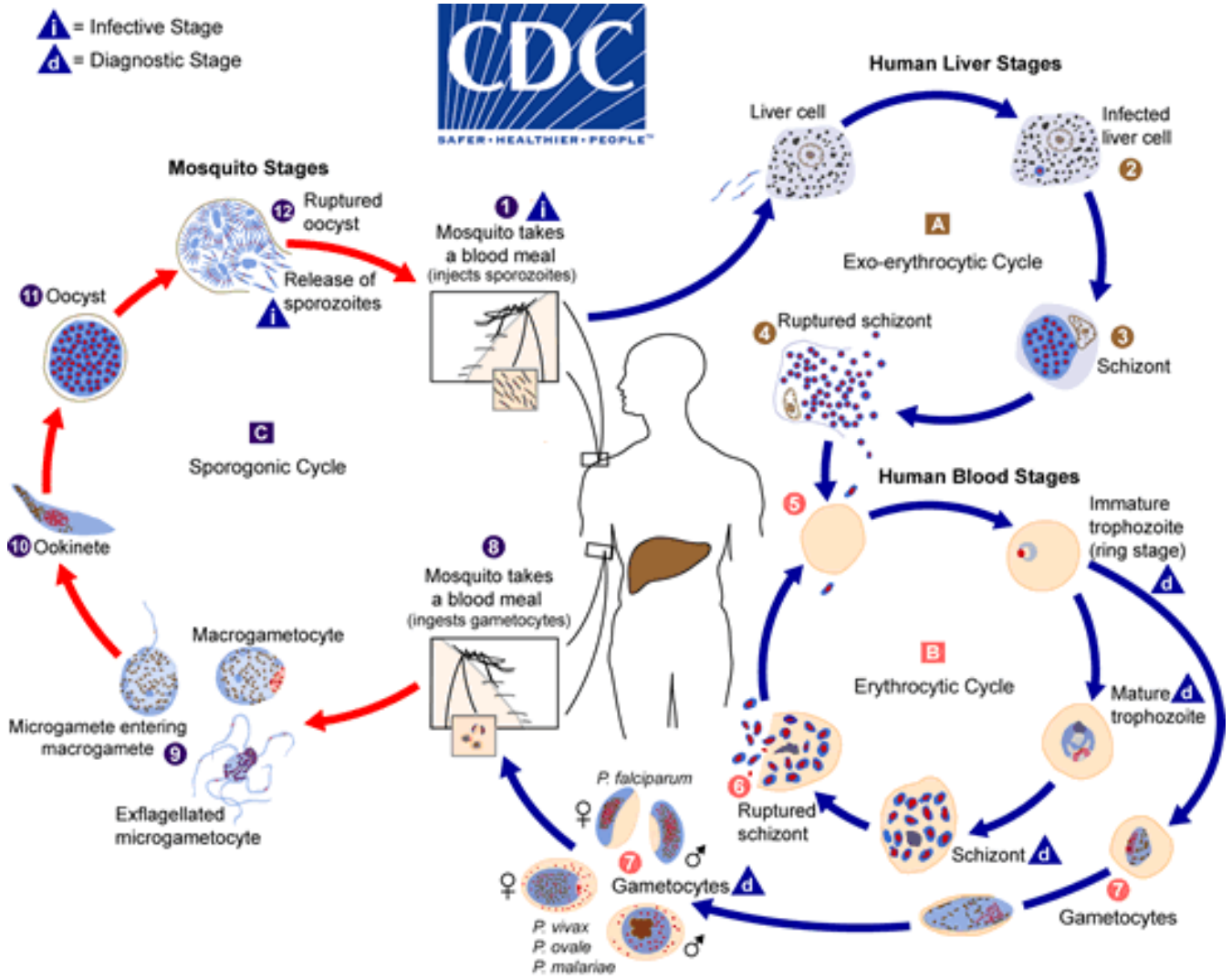
Malaria

- 4 main human ***Plasmodium* parasites** (*falciparum, vivax, malariae, ovalae*).
- Over 200 *Plasmodium* spp. globally, infecting birds, reptiles, and other mammals (rodents, bats, primates)

Distribution *Plasmodium falciparum*

Distribution *Plasmodium vivax*



Guerra et al. 2006. *Trends in Parasitology*

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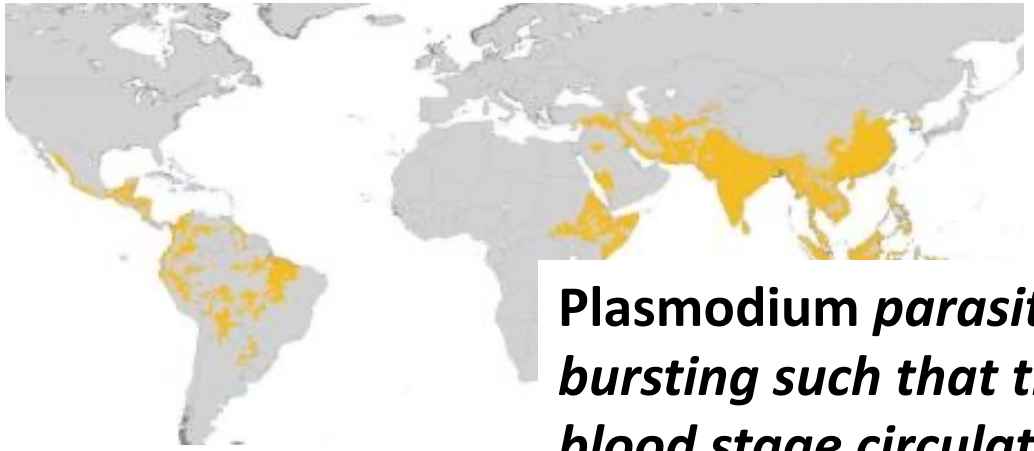

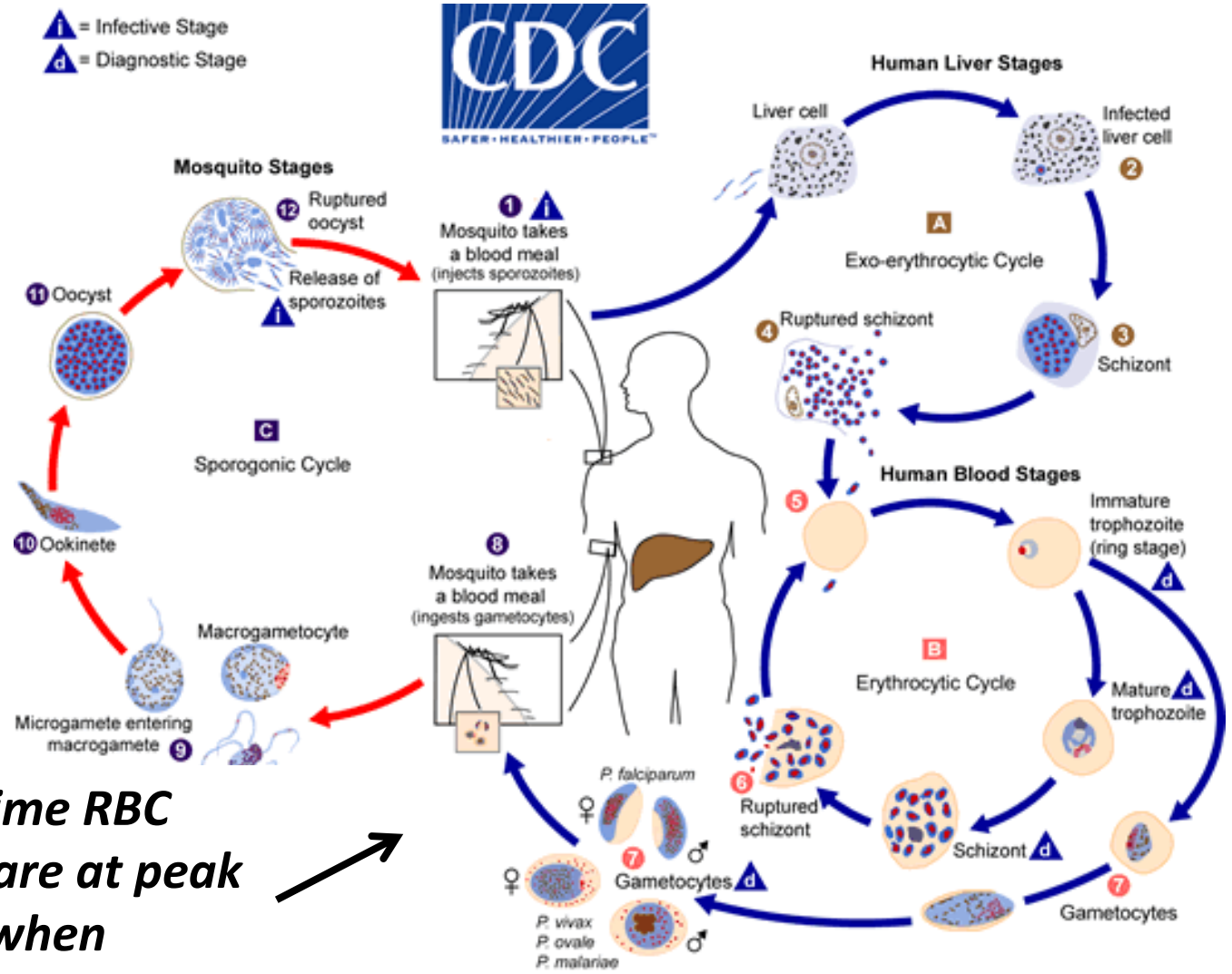

Plasmodium *parasites time RBC bursting such that they are at peak blood stage circulation when mosquito vectors are feeding at dusk!*

Guerra et al. 2006. *Trends i*

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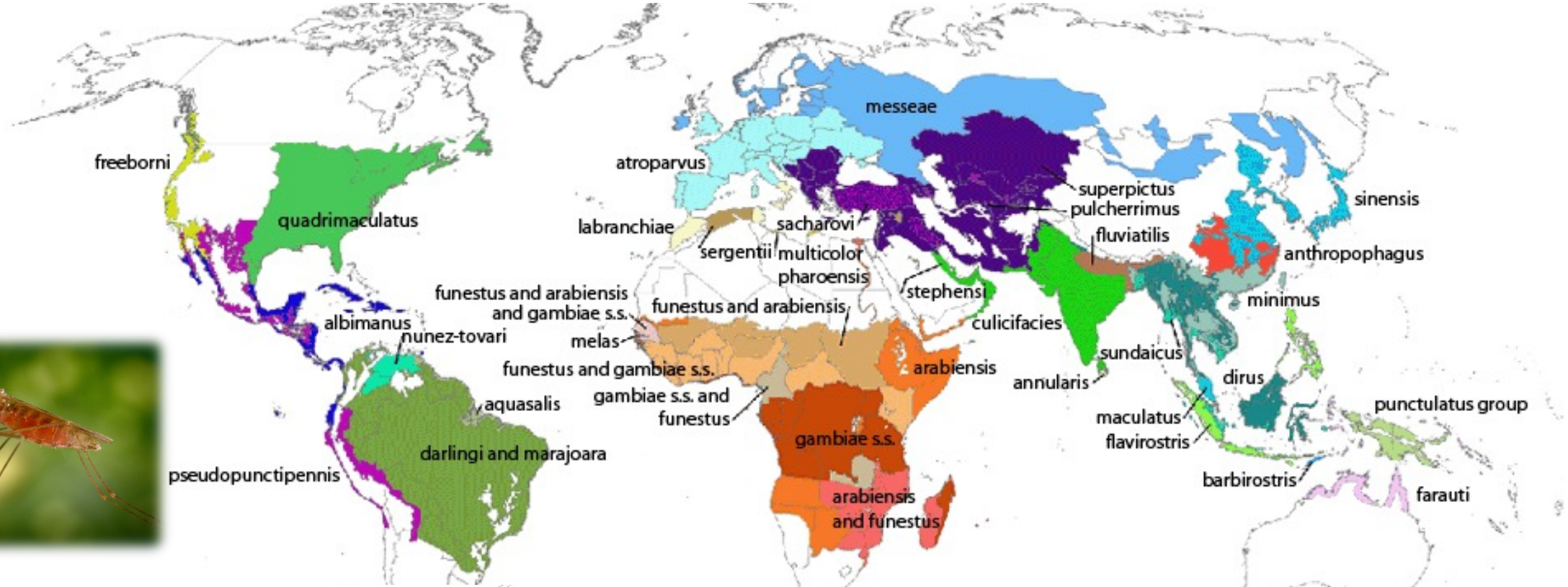
- ~30-40 *Anopheles* spp. most commonly implicated in human malaria transmission!



Kiszewksi et al. 2004. *ASTMH.*

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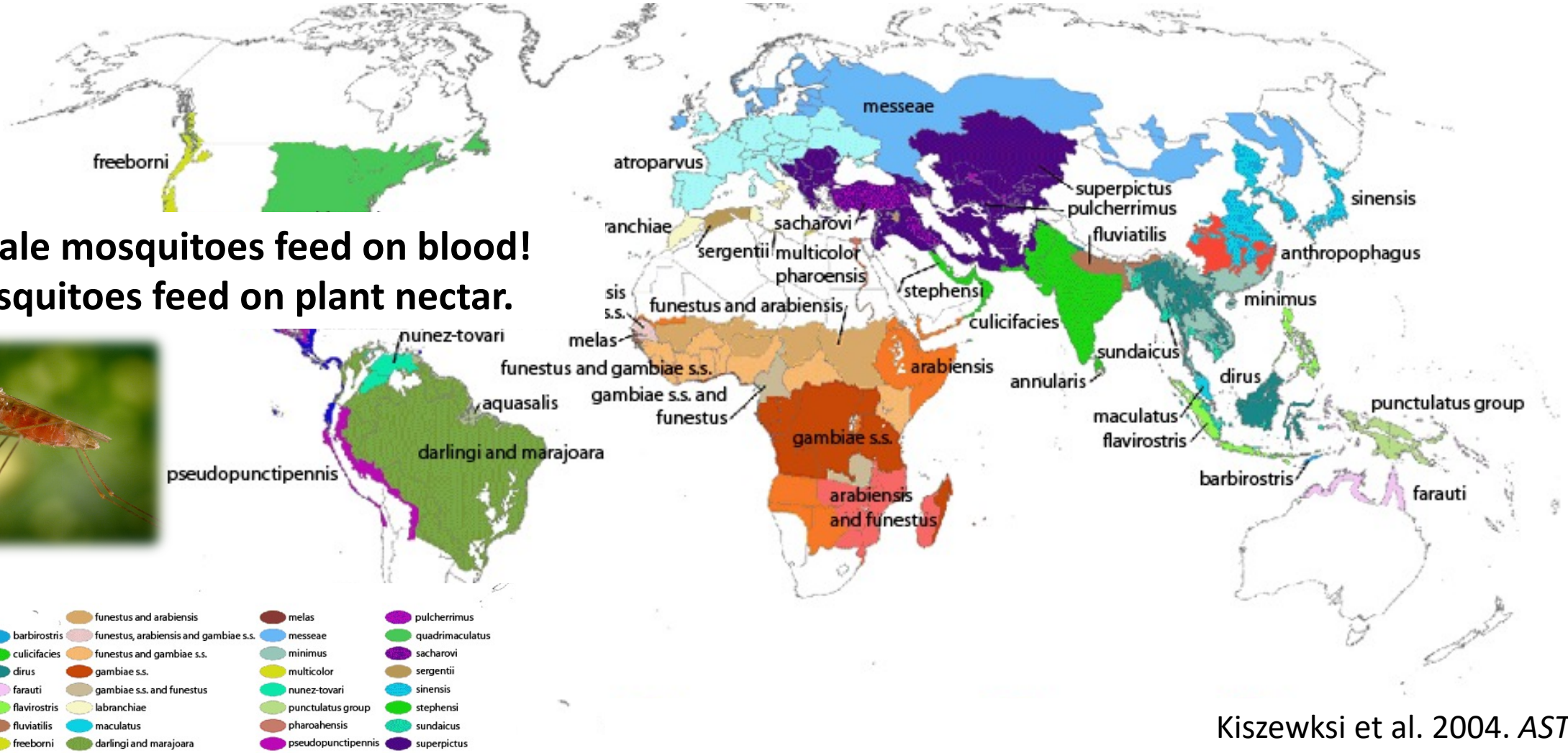
Only female mosquitoes feed on blood!
Male mosquitoes feed on plant nectar.



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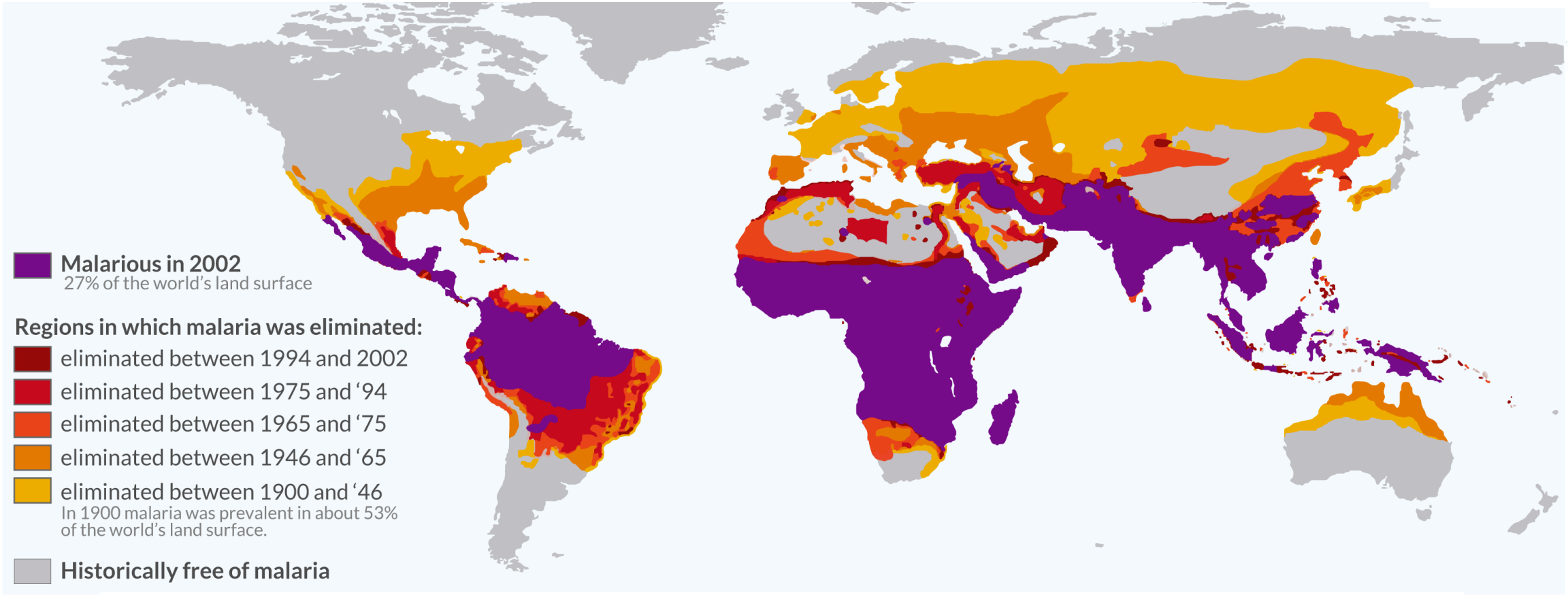
Malaria has been eliminated from many regions where it was previously endemic, including the US.



Still one of the leading causes of child mortality globally – responsible for about half a million childhood deaths a year, 80% in Africa.

OurWorldinData.org

Malaria models have played a critical role in public health policy for over a century.

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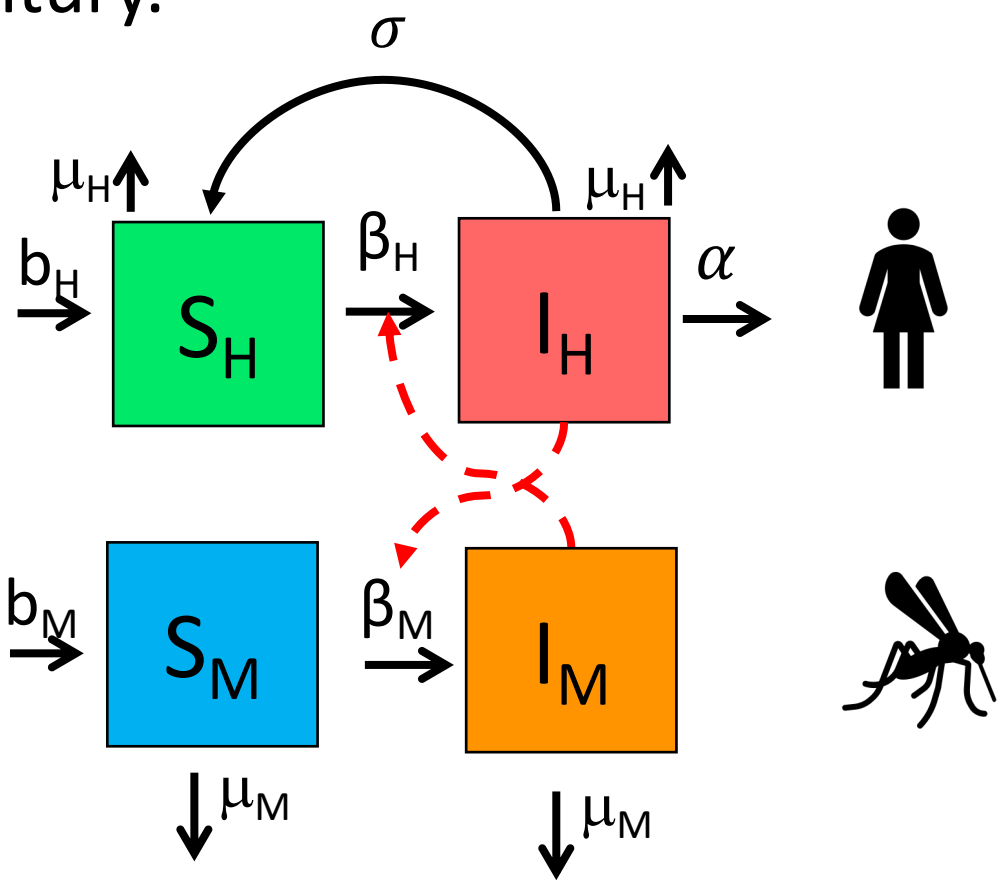
  - He had already won the 1902 Nobel prize in physiology and medicine for discovering the life cycle of avian malaria



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  - He implicated the survivorship of the female mosquito as the weakest link in the life cycle!

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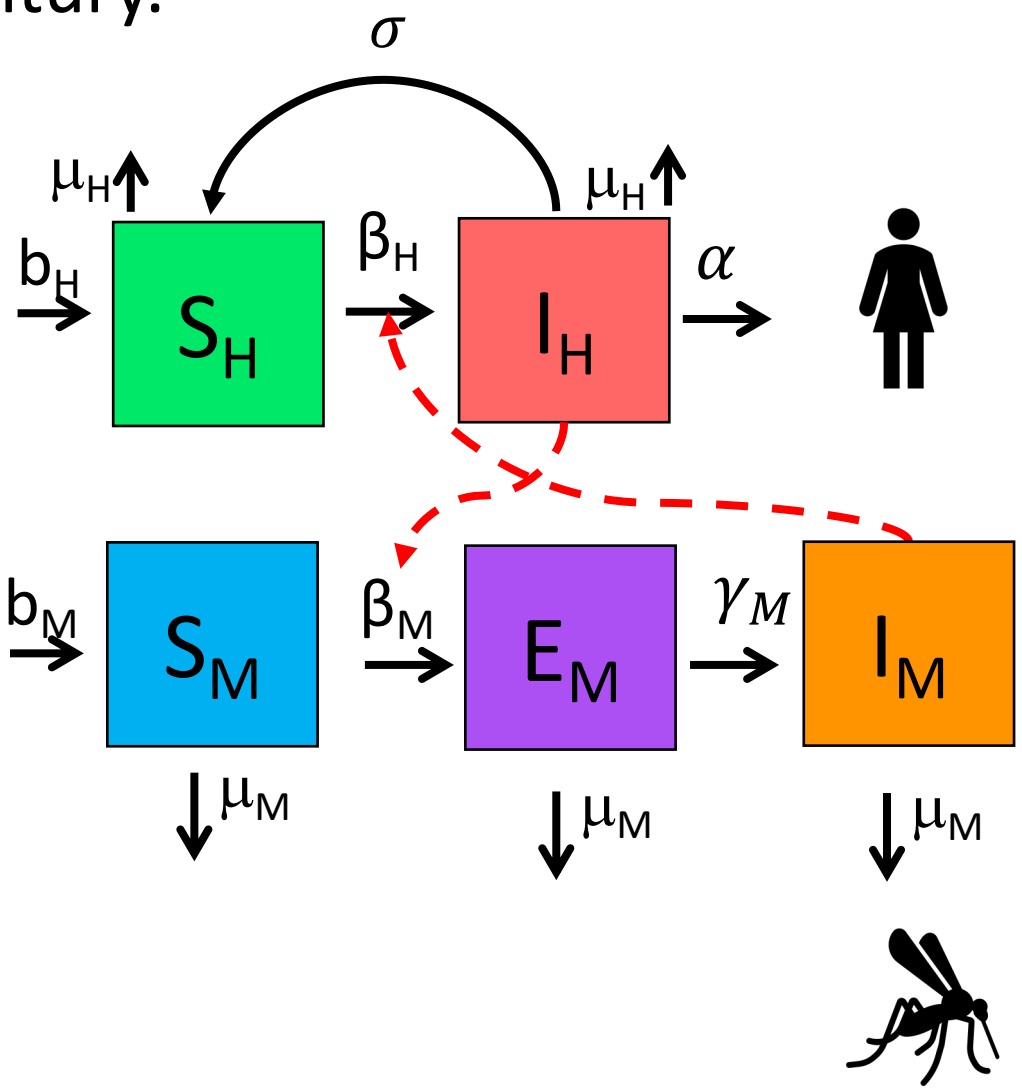

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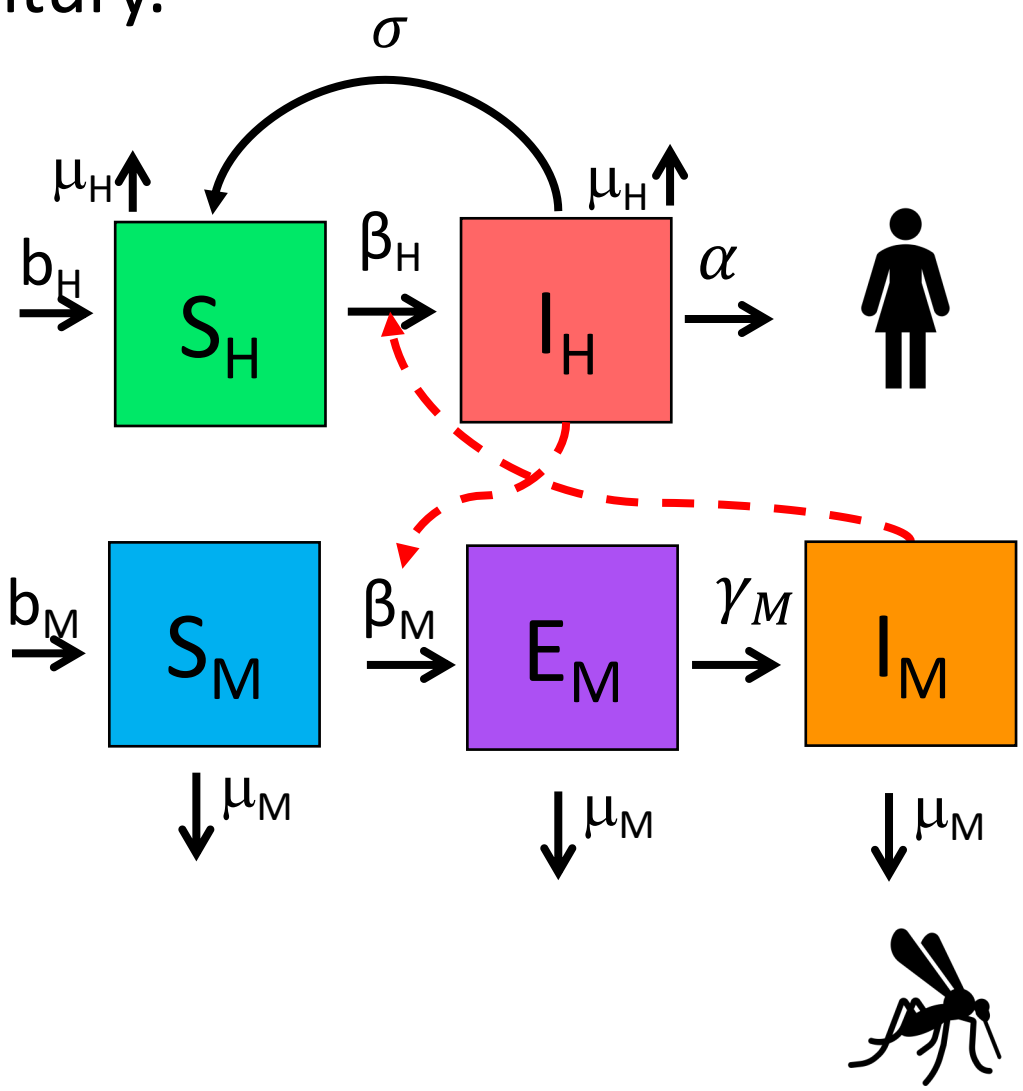

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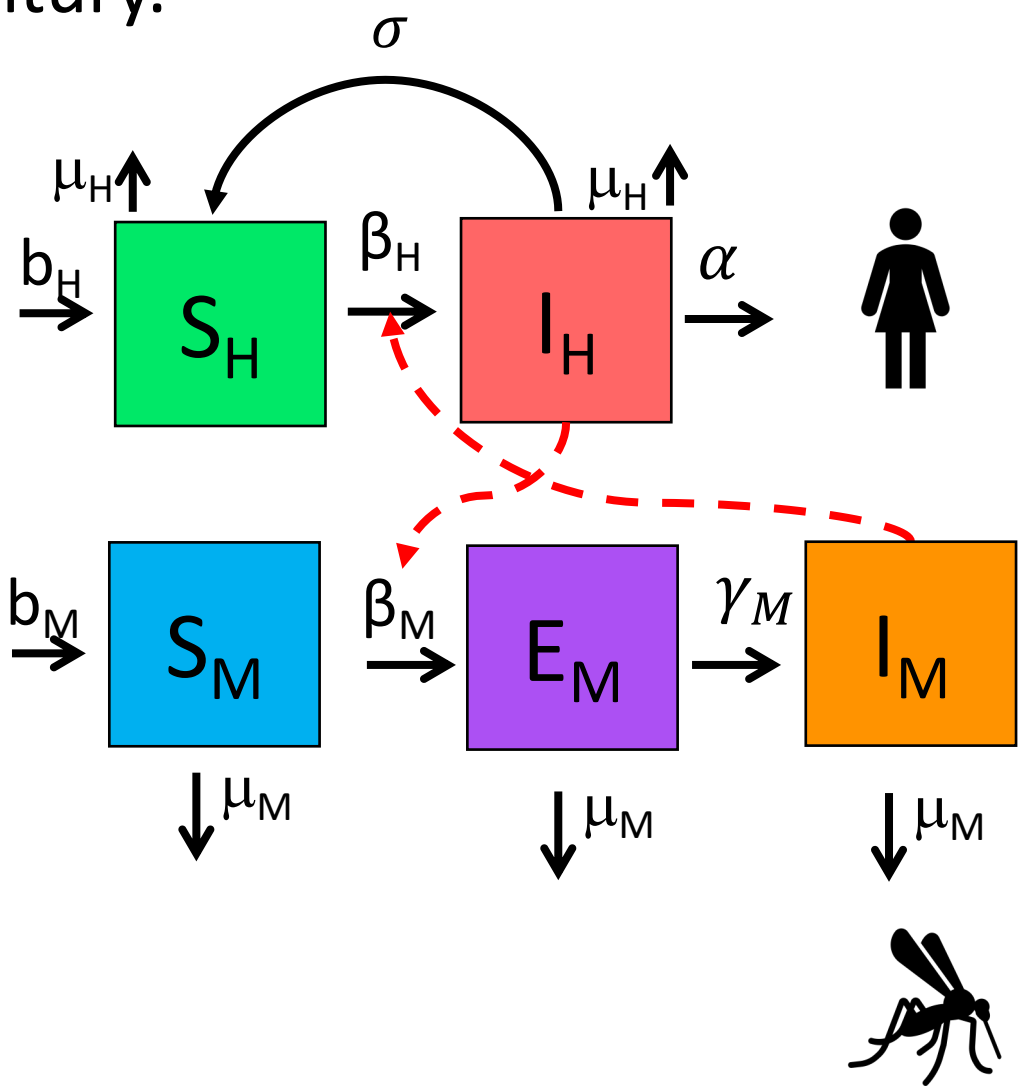

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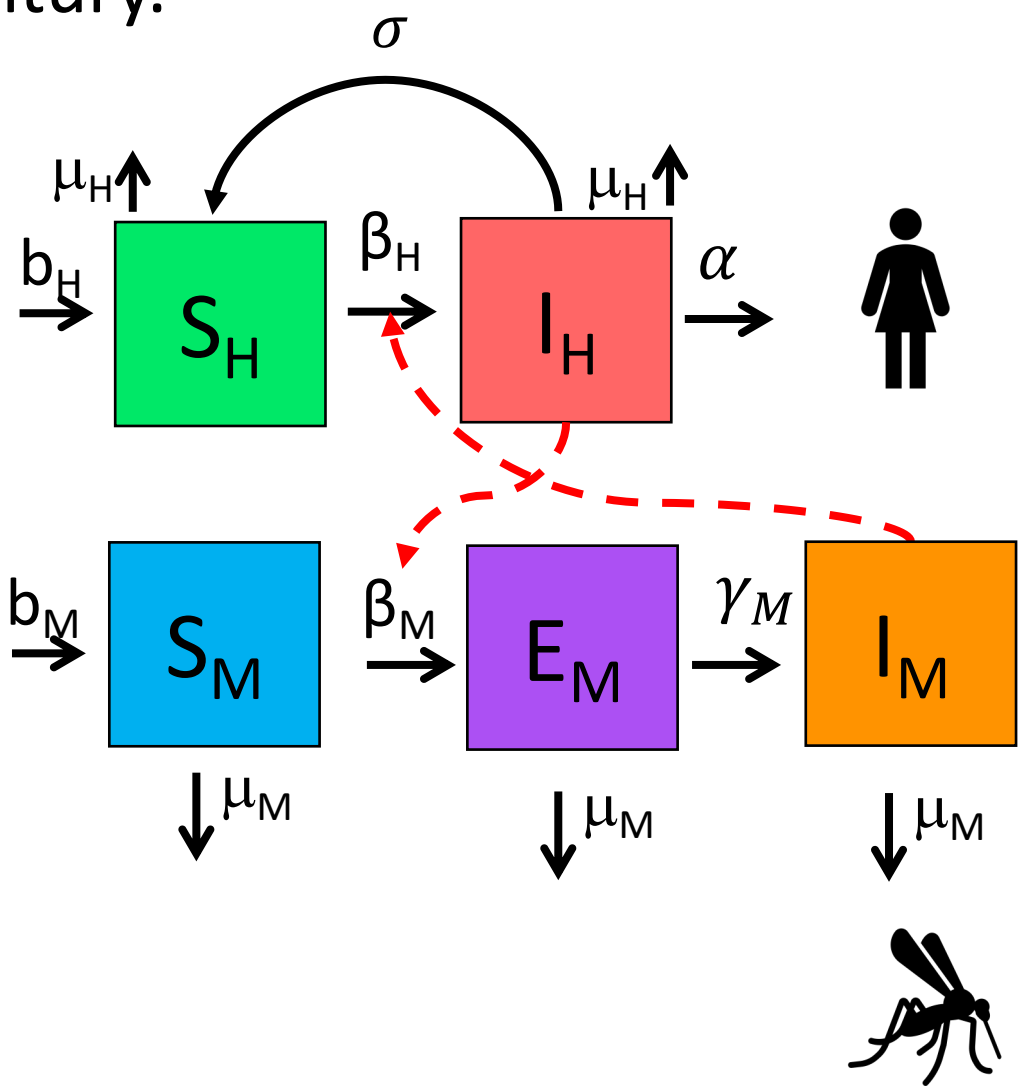

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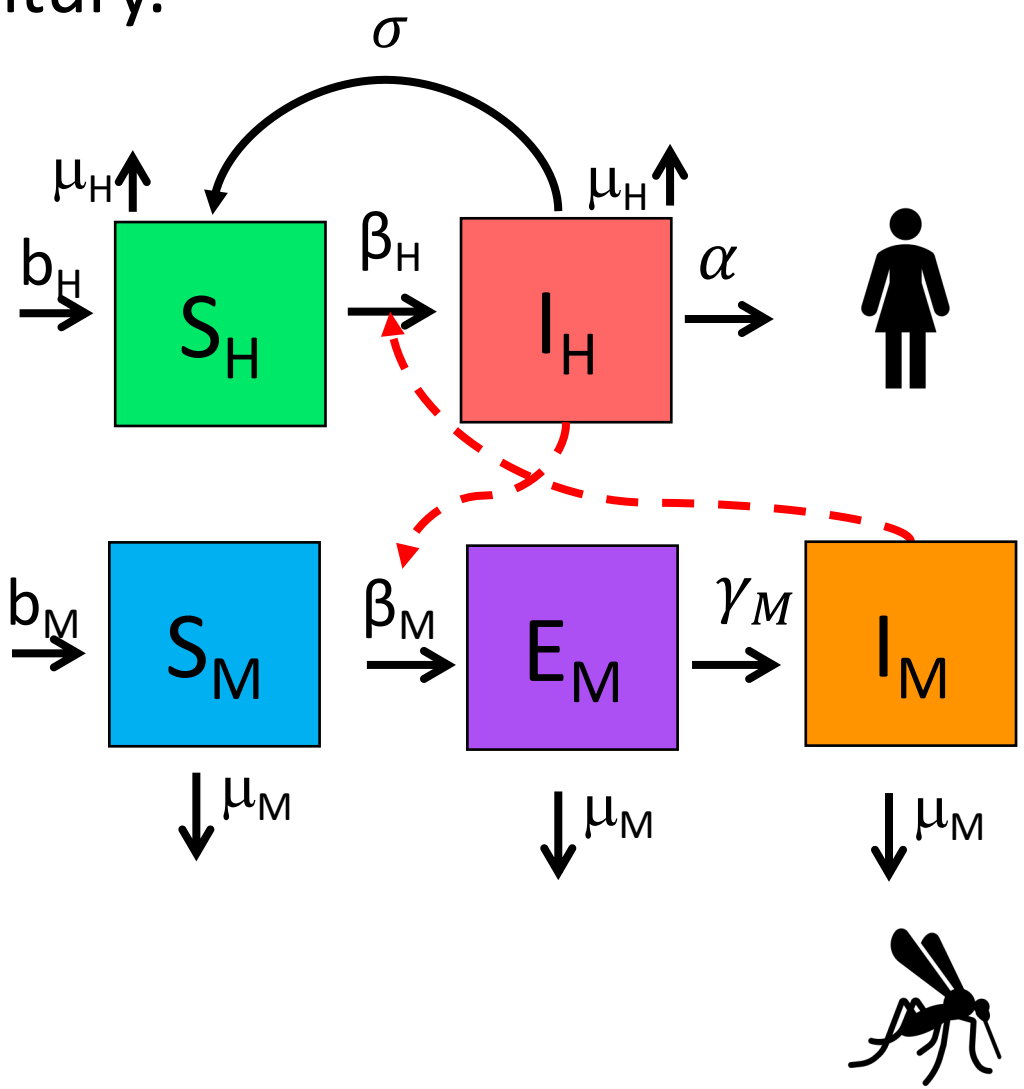

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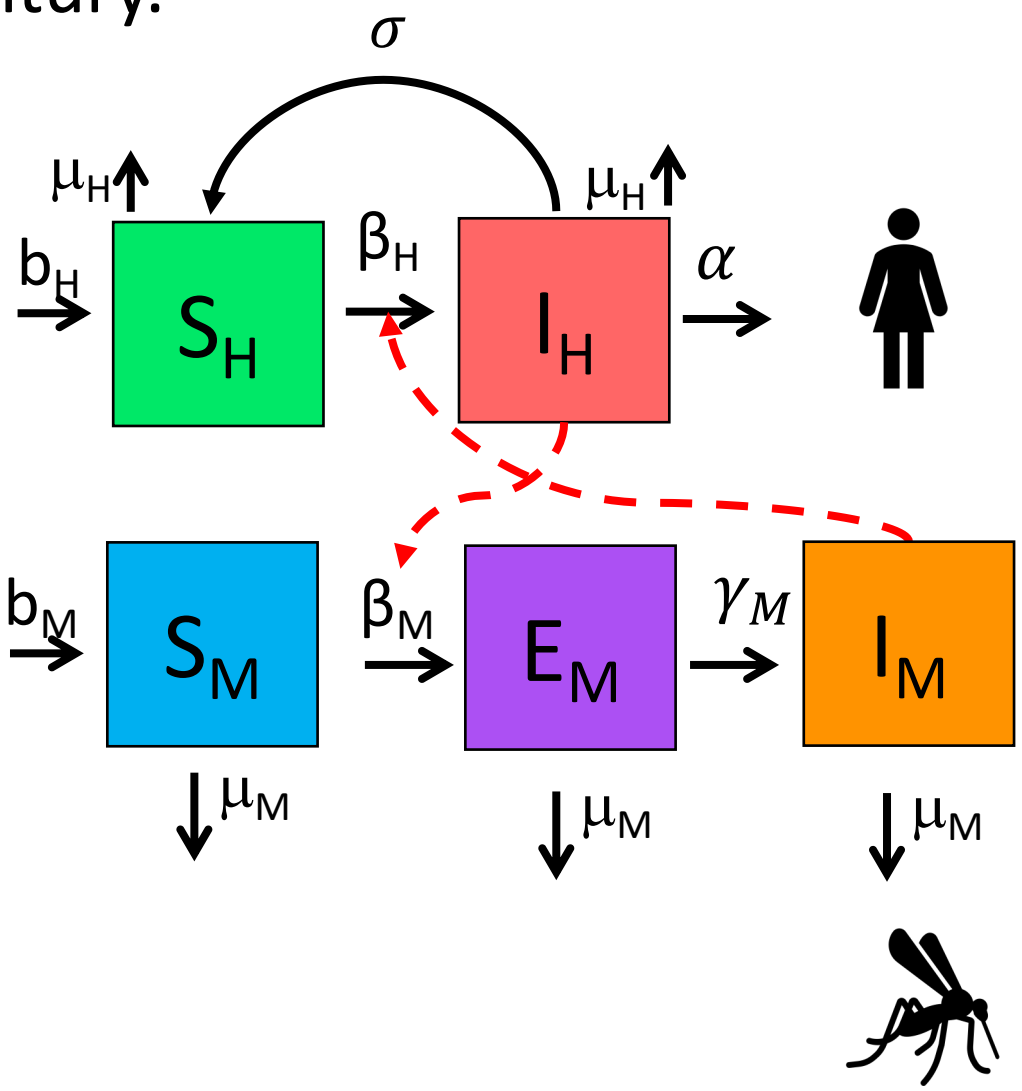

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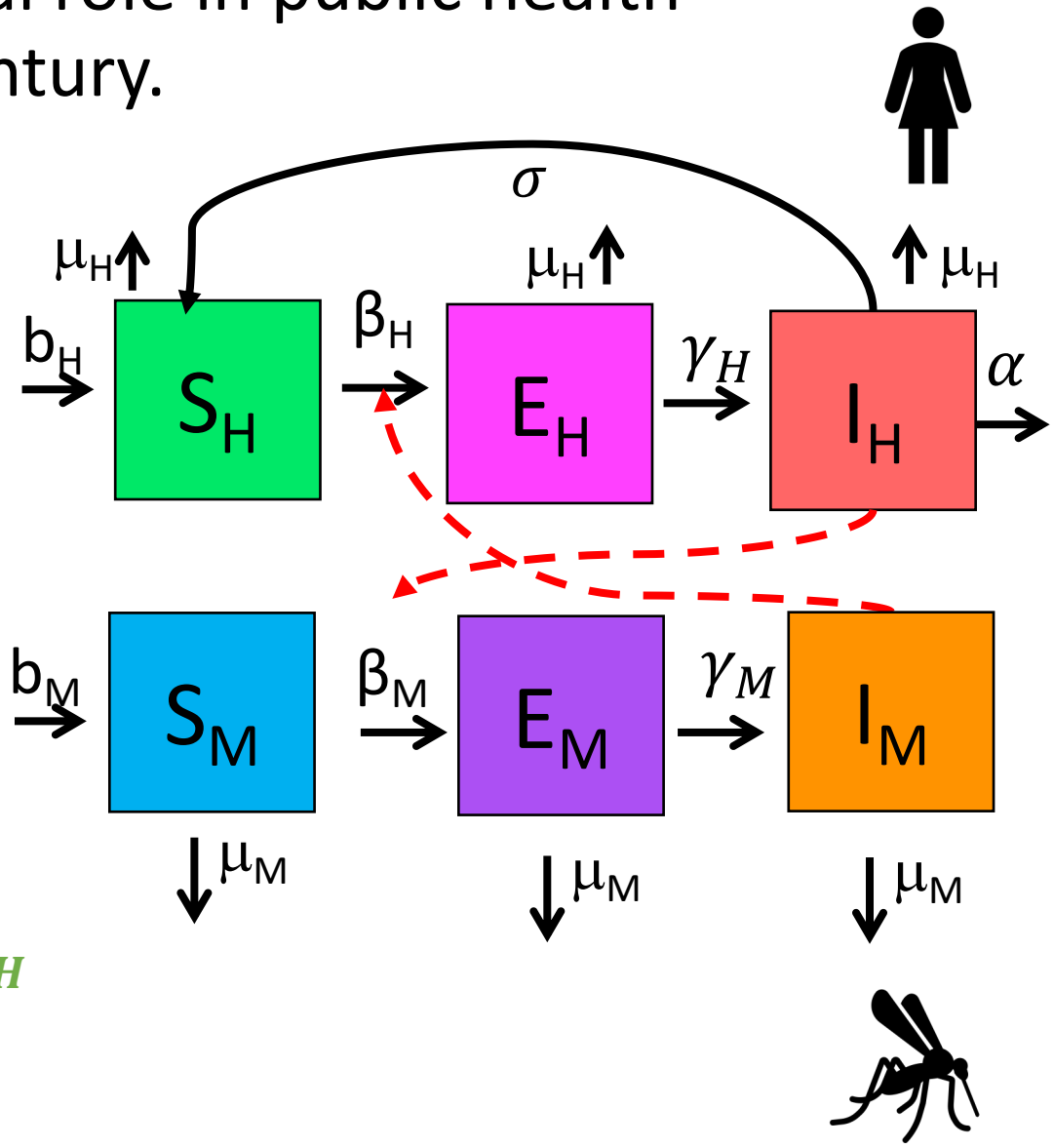
- 1991: Anderson and May extended model to show latency in the human population.



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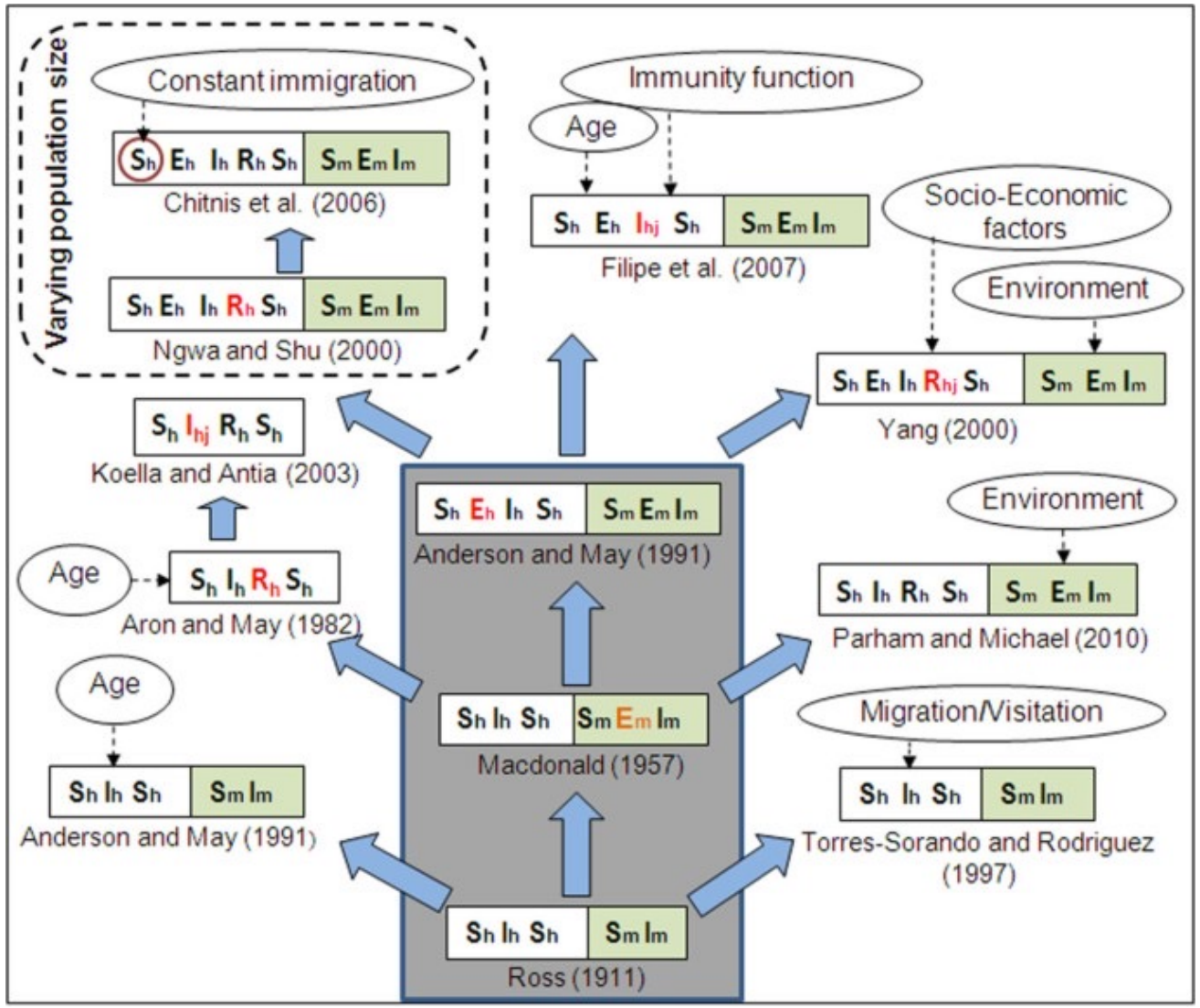
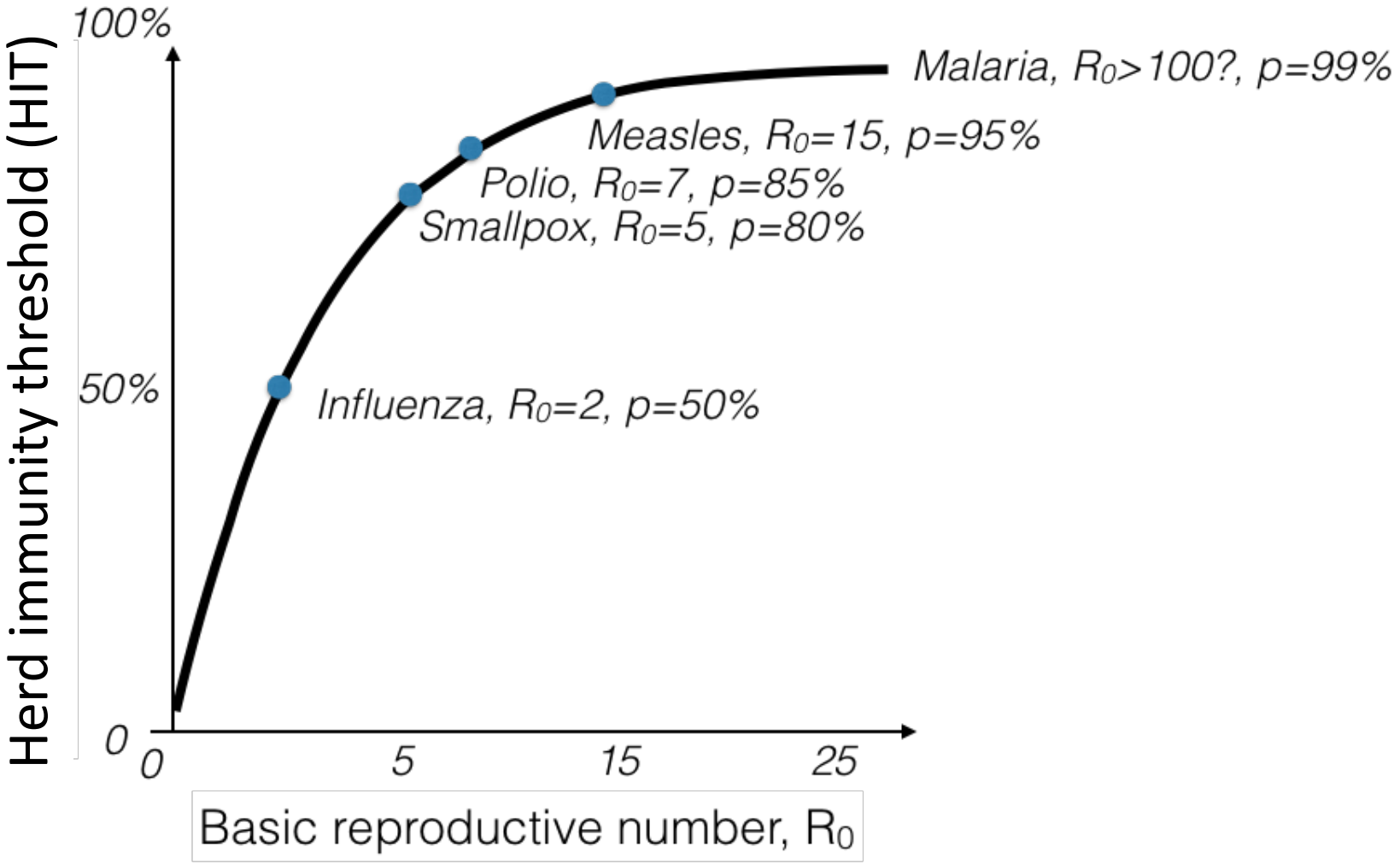


Mandal et al. 2011. *Malaria Journal.*

Challenges to malaria elimination

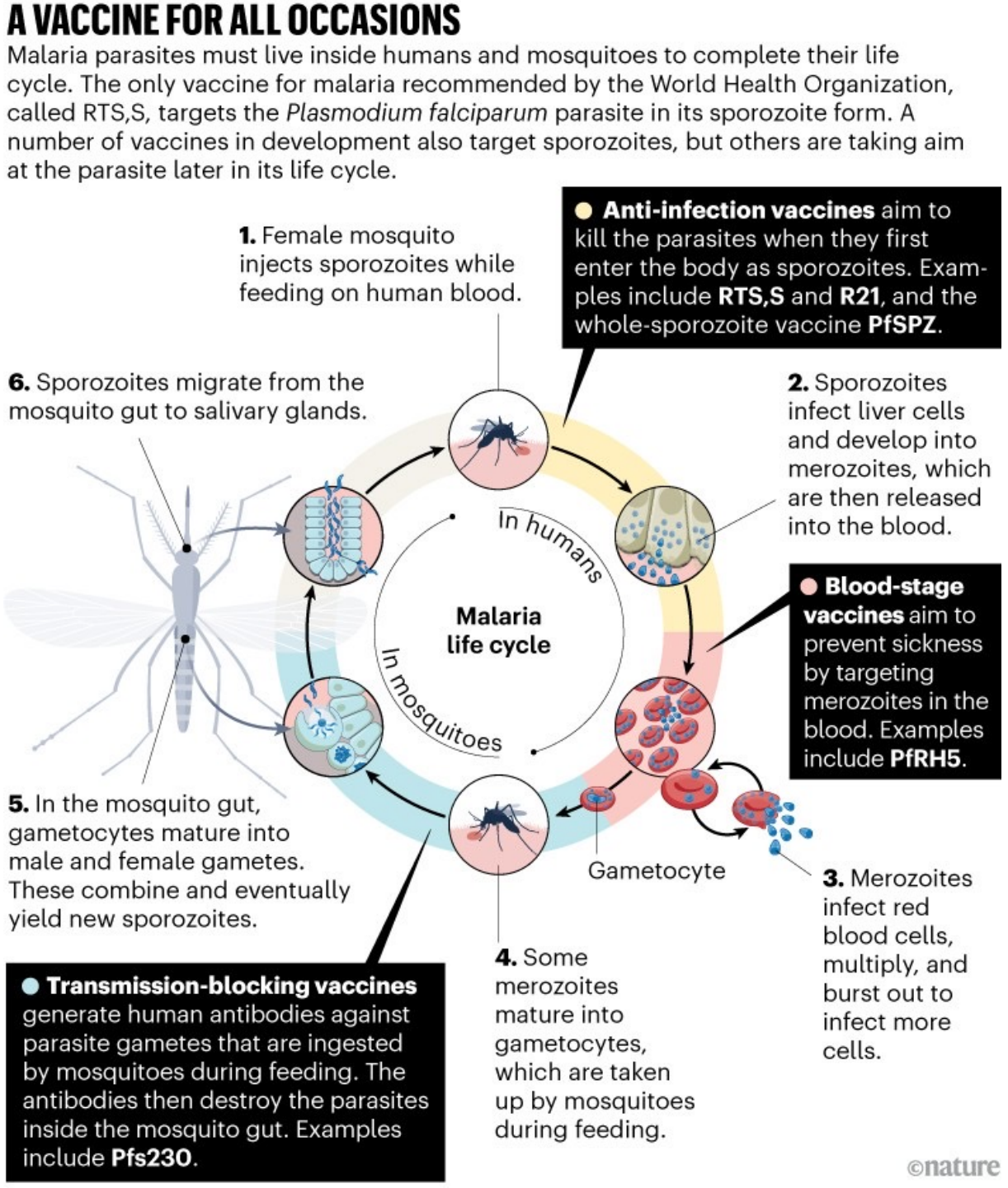


Challenges to malaria elimination?

- High parasite diversity: sexual reproduction in 4+ *Plasmodium* species
  - Fast evolution of resistance *(e.g. to drugs)*
- Many possible vectors! Potentially additional possible reservoirs!
- Latent cases as burden is reduced
- Vaccine candidates: what life stage to target?

Malaria vaccines

- Only two currently licensed
- *Mosquirix*/RTS,S pre-erythrocytic vaccine licensed in 2022
  - Requires at least 3 doses in children <2
  - Does not eliminate pathogen but reduces severe malaria burden and burden of hospitalization by ~30%
- *R21/Matrix-M* pre-erythrocytic vaccine licensed in 2023
  - Requires at least 3 doses in children <2
  - Does not eliminate pathogen but reduces severe malaria burden and burden of hospitalization by 77%



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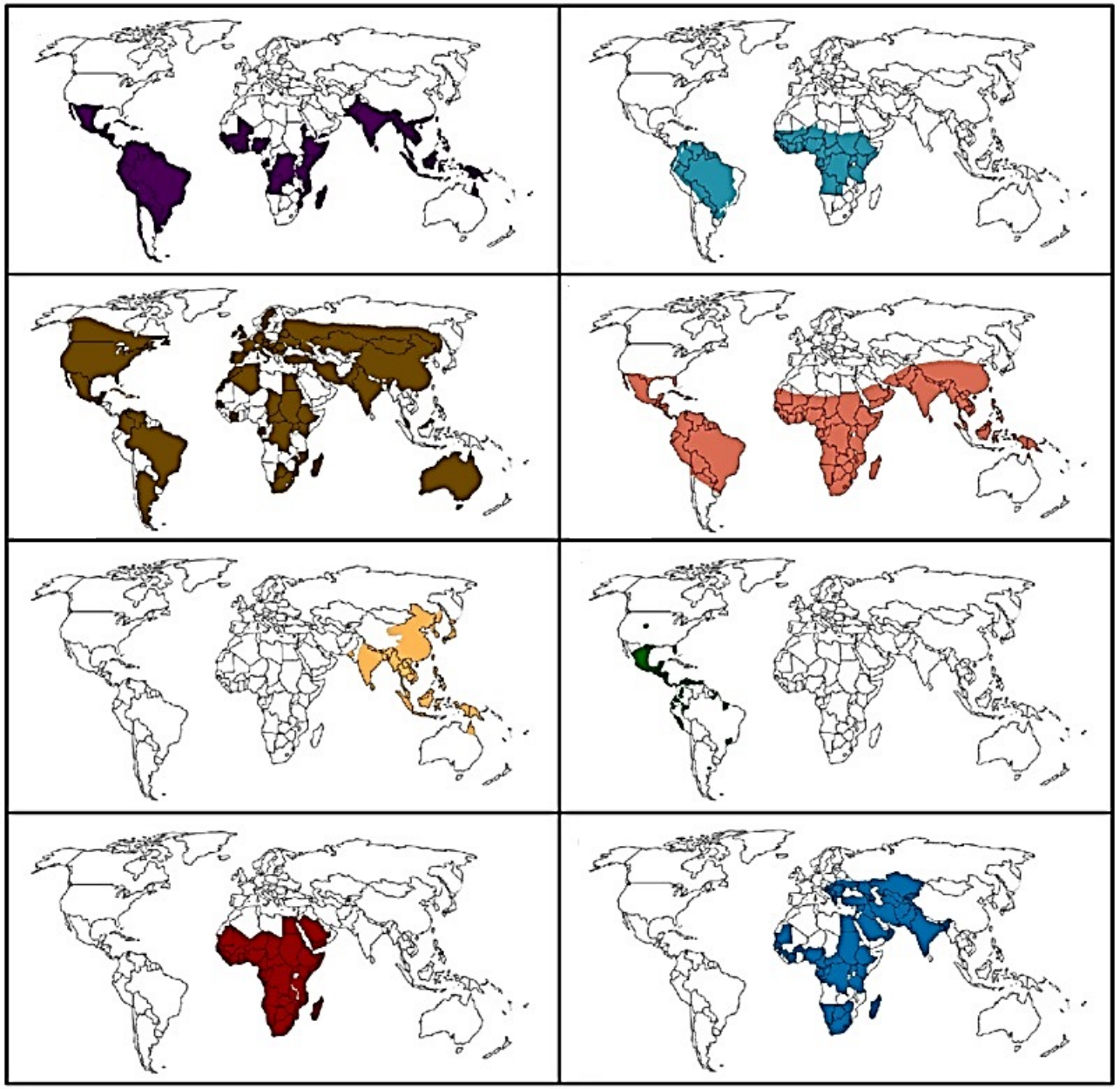
Important arbovirus distributions

Aedes spp.

Dengue virus



Yellow fever virus

Aedes spp.

Culex pipiens

West Nile virus

Chikungunya virus

Aedes spp.

Culex pipiens

Japanese encephalitis virus

Venezuelan equine encephalitis virus

Culex -> *Aedes*

Culex and *Aedes*

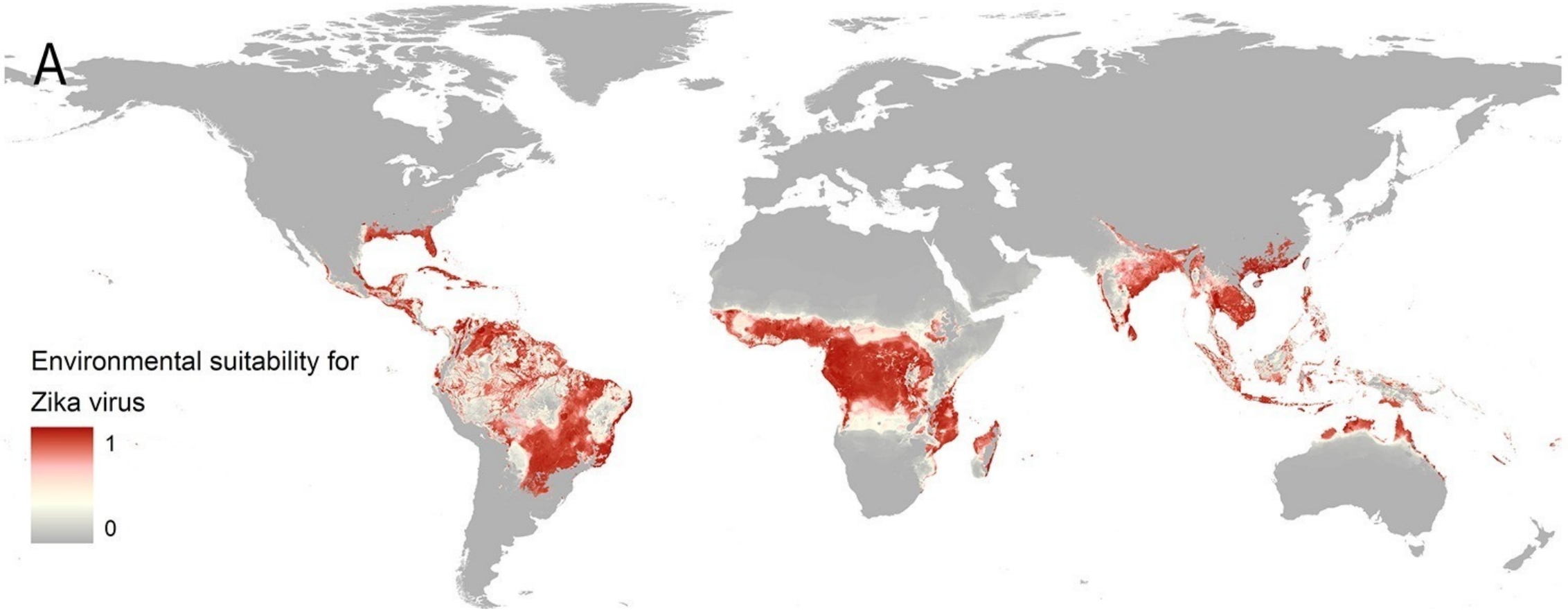
Rift-Valley fever virus

Crimean-Congo hemorrhagic fever virus

Hyalomma ticks

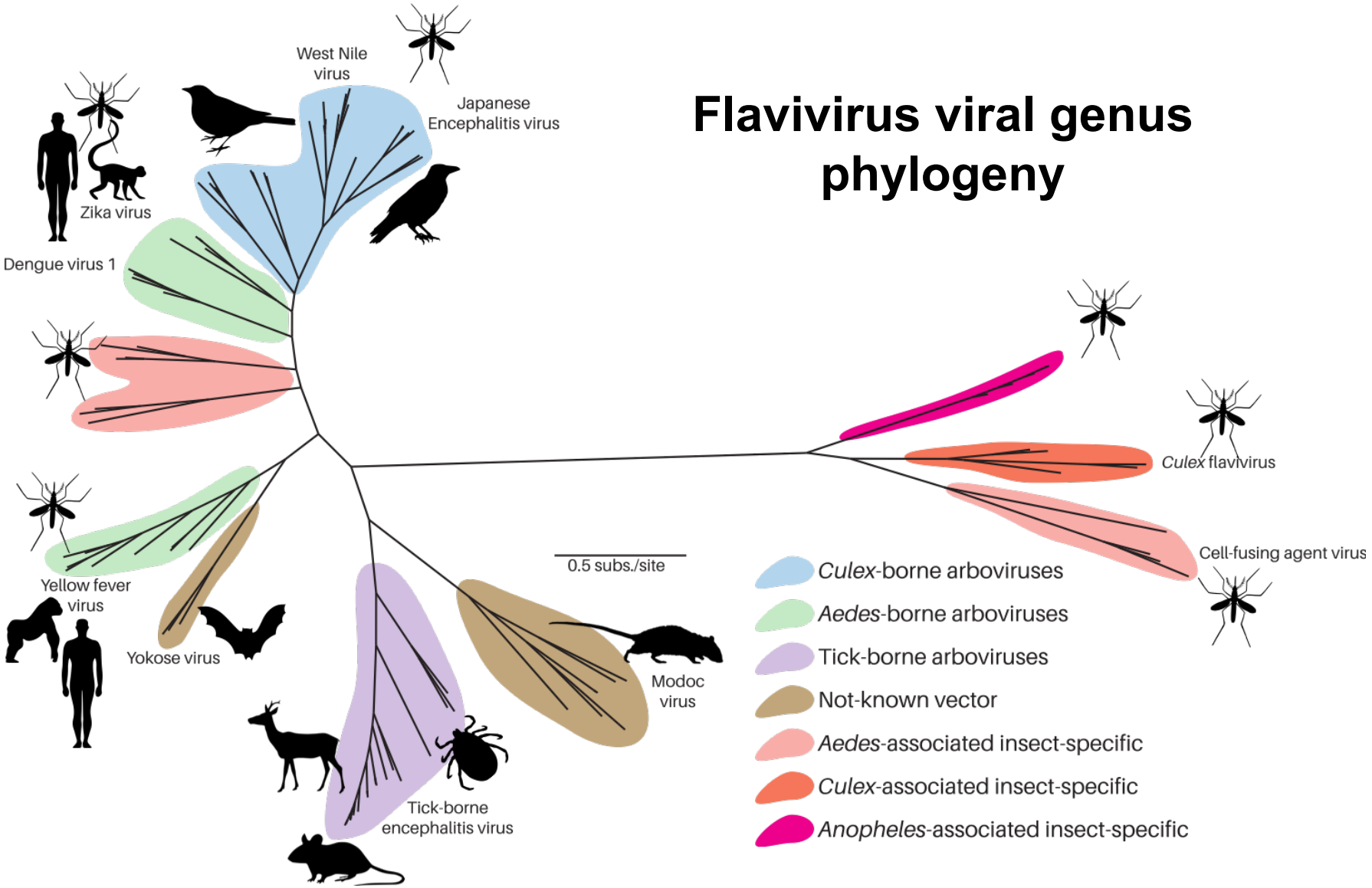
Iranpour. 2016. *Expert Reviews in Molecular Medicine*

Zika is also vectored by *Aedes aeygpti* and its relatives



Messina et al 2016. *eLife*

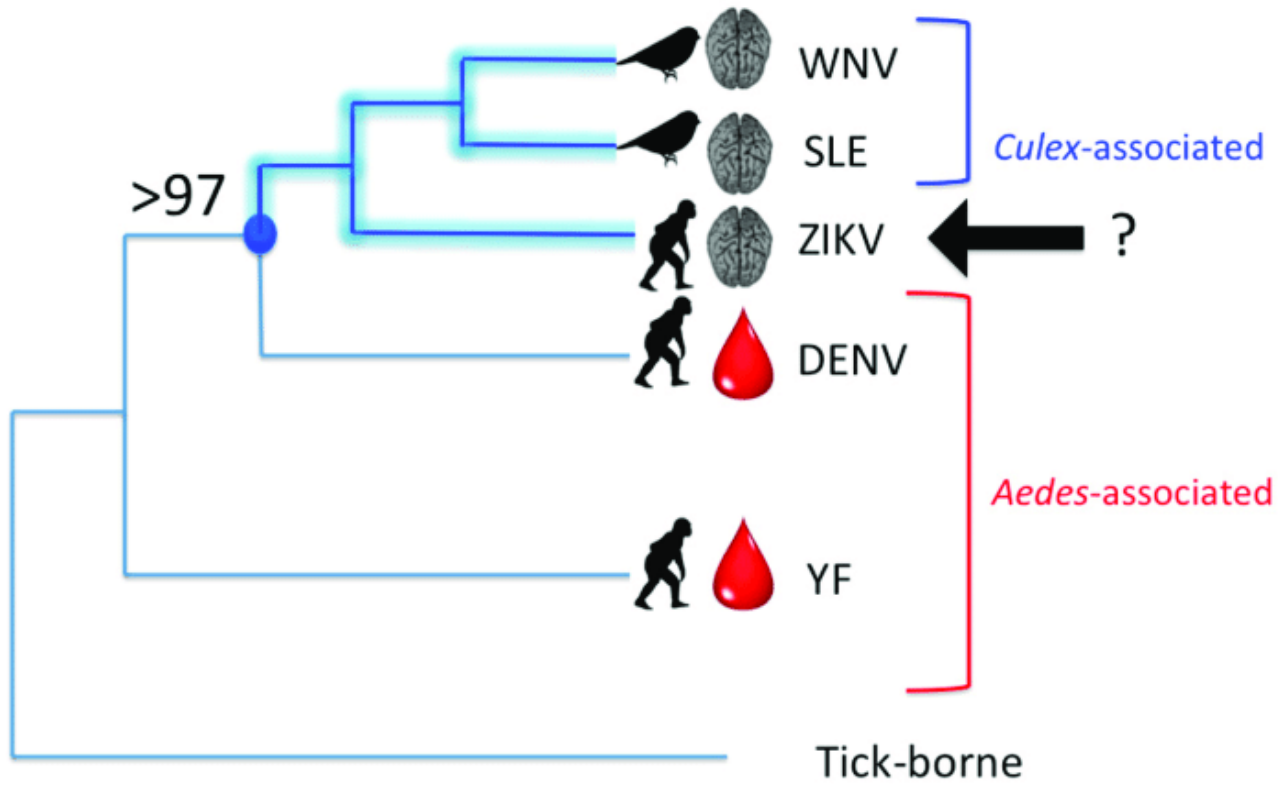
Arboviruses infect a wide range of hosts and vectors

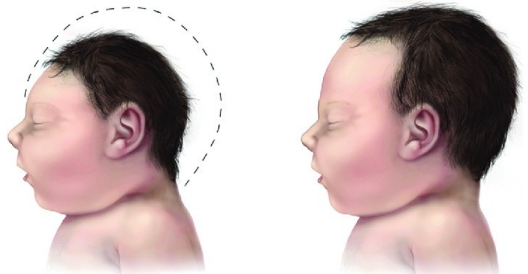


Flavivirus viral genus phylogeny

Sebastian Lequime. 2020.

Arbovirus disease progression



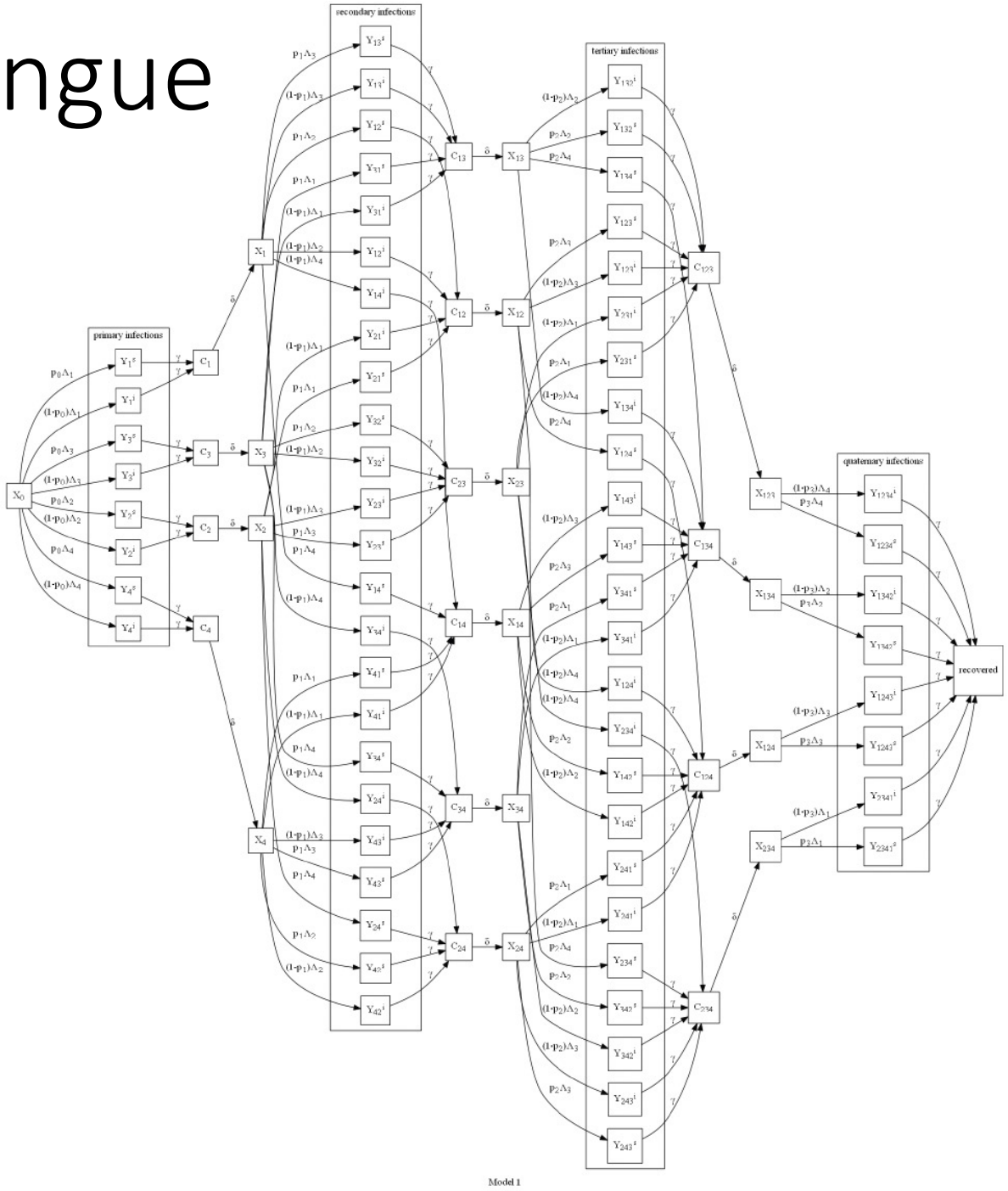


Hunter. 2017. *Frontiers in Micro*

Dengue fever

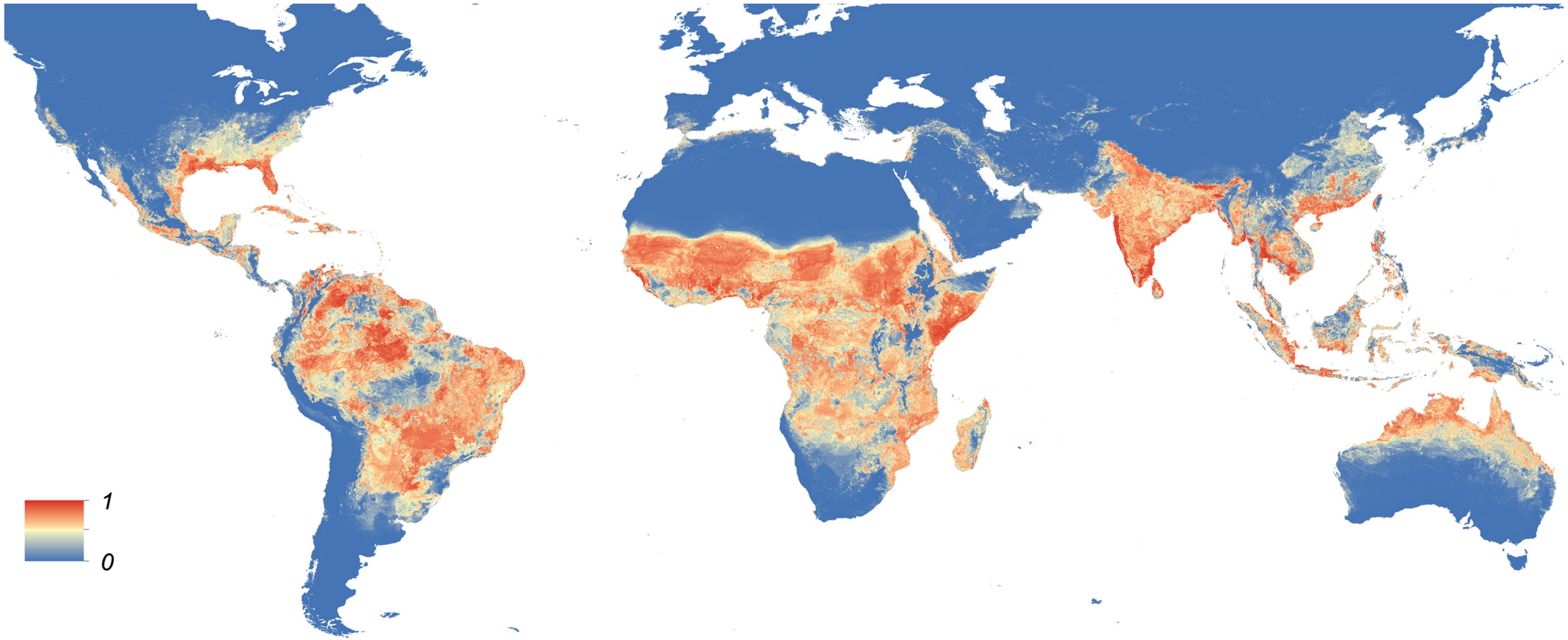
- Mosquito-borne disease caused by one of four known serotypes of dengue virus (DENV-1, -2,-3,-4)
- A small proportion of cases develop into dengue hemhorrhagic fever (bleeding, blood plasma leakage) or dengue shock syndrome (dangerously low blood blood pressure)
- Most severe cases occur in secondary infections resulting from antibody-dependent enhancement (ABD), a phenomenon whereby pre-existing immunity to a single serotype facilitates infection by a subsequent serotype
- 40% of the world's population resides in dengue-endemic
- Only one licensed vaccine: Dengvaxia (tetravalent vaccine which confers immunity to all 4 serotypes simultaneously
  - Licensed in 2016 but controversy developed after severe cases developed in those who were previously naïve in Philippines)

Modeling dengue (at its most complex!)



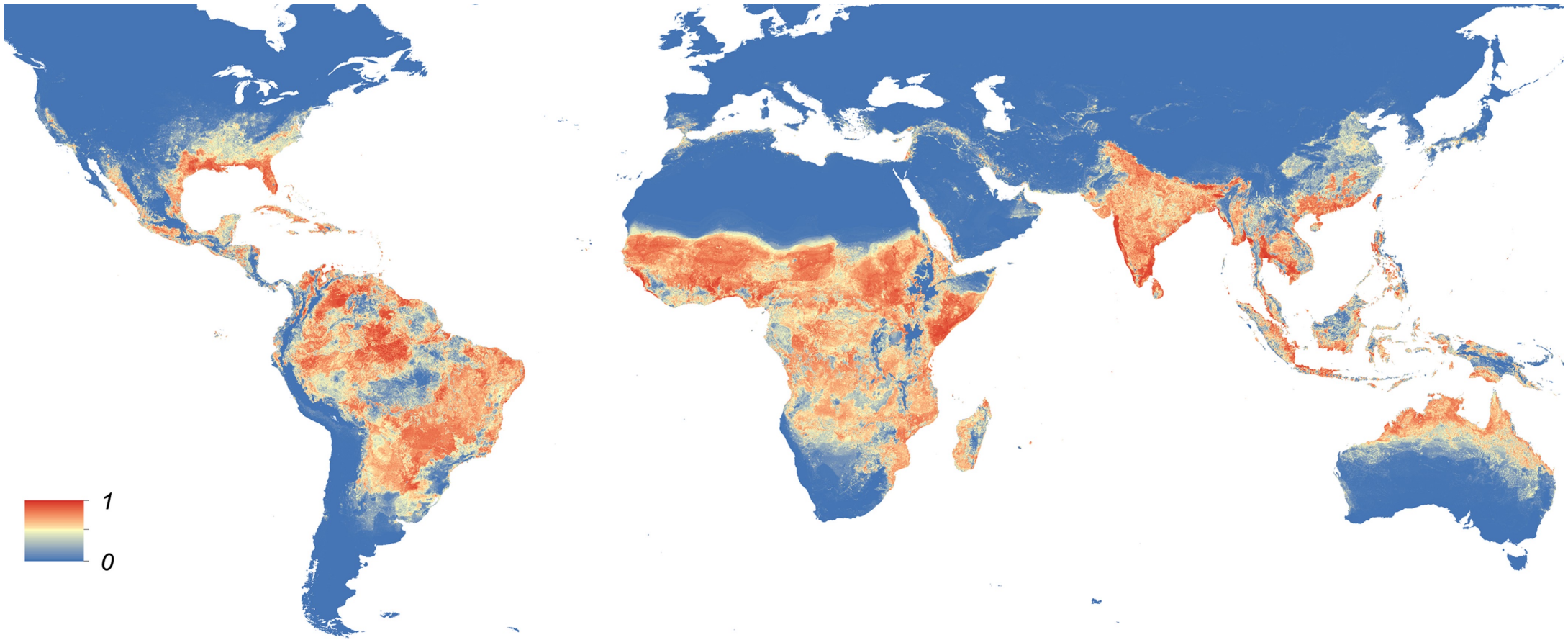
Alexander et al. 2021. *PNAS.*

Global distribution of *Aedes aegypti*



Kraemer et al. 2015

Global distribution of *Aedes albopictus*



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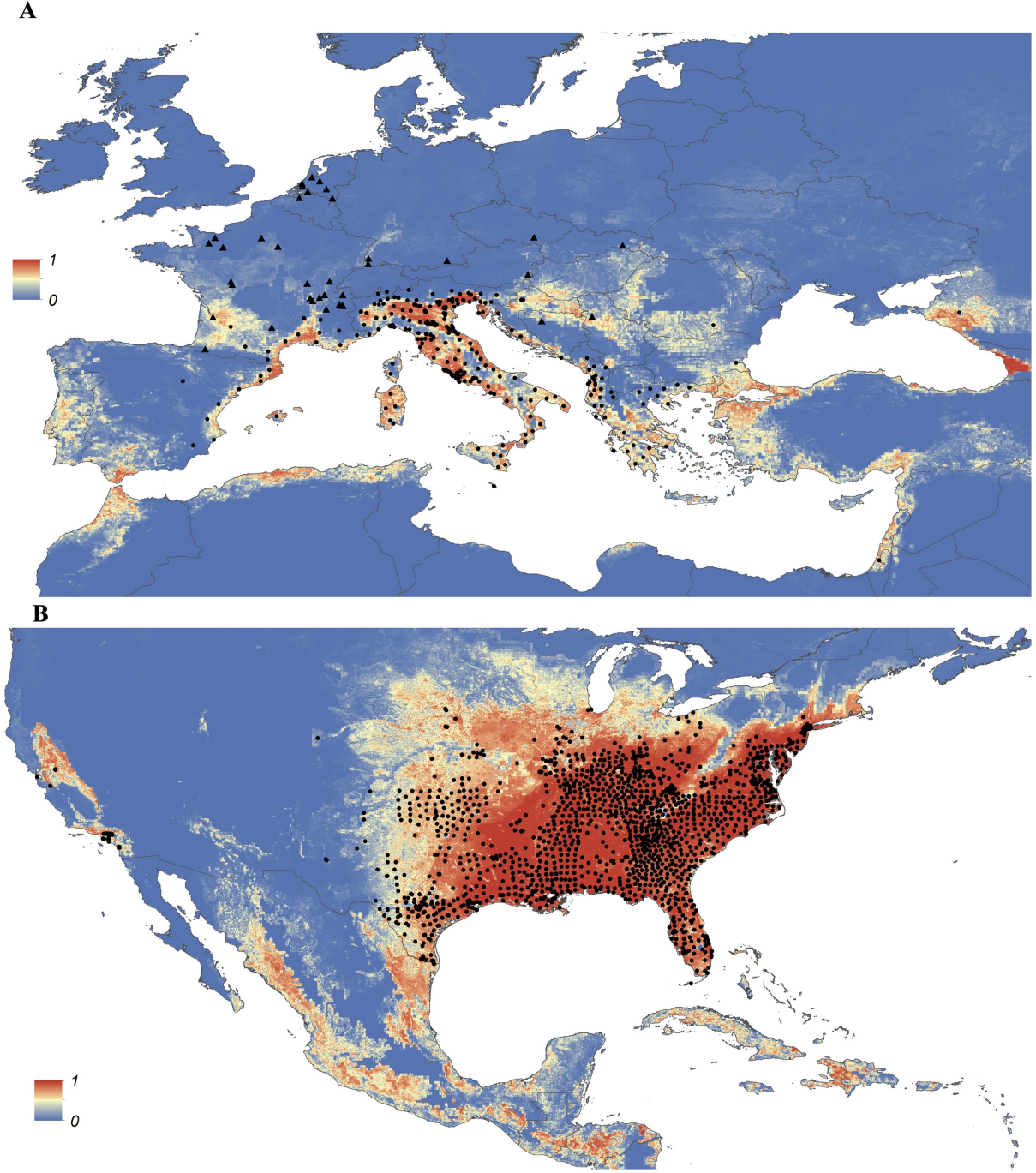


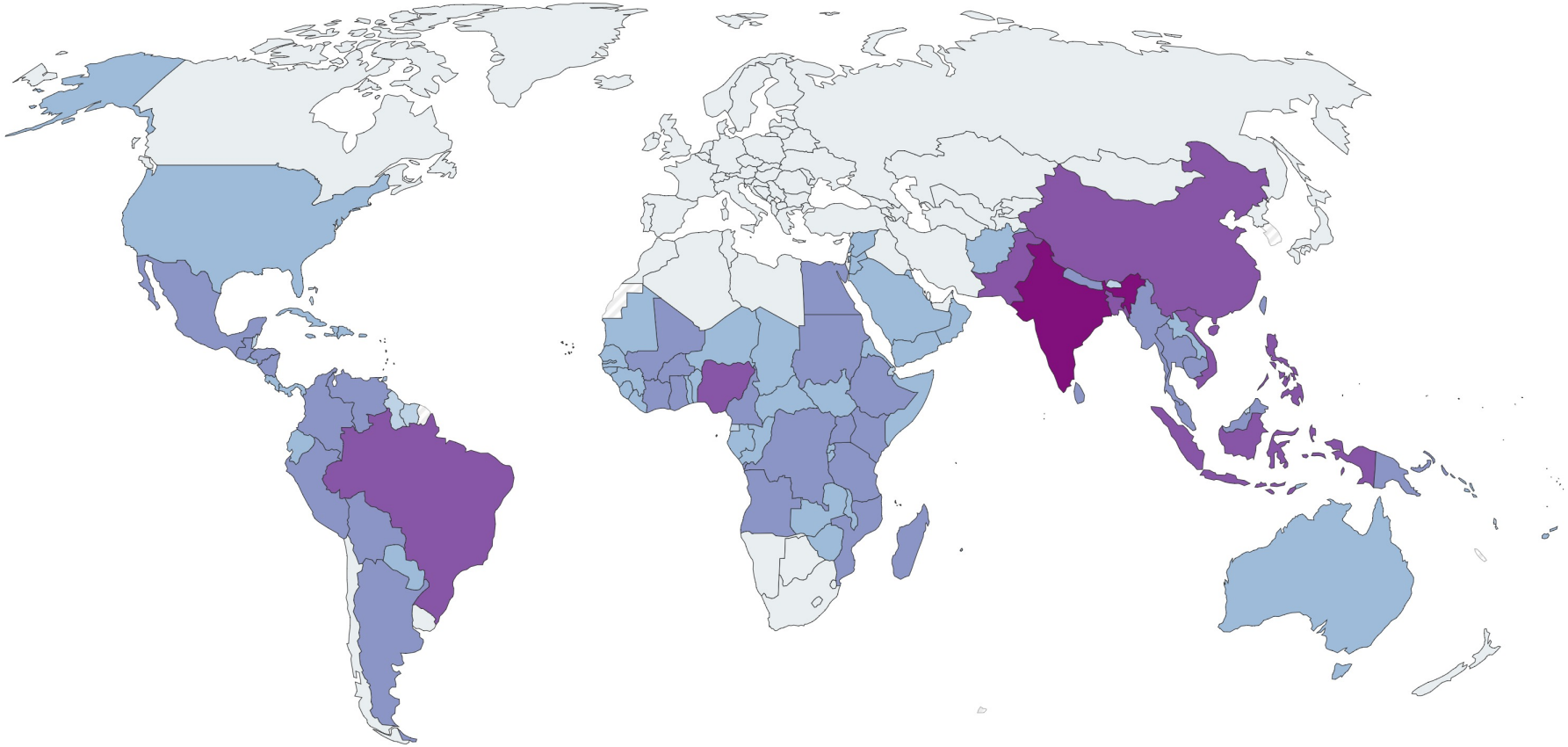
Detailed probability of occurrence of *Aedes albopictus* in Europe and US, areas where the mosquito is most rapidly expanding its range

Kraemer et al. 2015

Dengue fever infections, 2019

Our World in Data

Estimated annual number of new dengue infections. Dengue is a viral infection transmitted through the bite of infected mosquitoes; symptoms include fever, headaches, and nausea. Most infections are asymptomatic or mild, but dengue can occasionally be severe or fatal.



Data source: IHME, Global Burden of Disease (2019)

OurWorldInData.org/burden-of-disease | CC BY

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Plague is BOTH vector-borne and zoonotic!