# The intra-vector viral dynamics challenge a common assumption in vector-borne diseases modeling

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Arboviruses = threat to public and veterinary health. -> Intra-vector viral dynamics (IVD) is key element of arboviruses transmission. BUT -> Most of vector-borne disease models use the mean of extrinsic period of incubation (EIP) and IVD has not been considered so far. Current models assume then an exponential distribution of durations in EIP whithin mosquitoes population.

## Is this exponential distribution assumption of durations always applicable?

#### **EXPERIMENTAL DATA**

 $\rightarrow$  Data from blood meal mosquito infection experiments.

Infection states : HI : Infectious Human

**HS** : Healthy Human



Experimental protocol :

**1**) Feeding of mosquitoes with

Viruses	Mosquito species and origin
CHIKUNGUNYA <sup>[3]</sup>	Aedes albopictus
→ CHIKV, alphavirus, strain 06.21 from Indian Ocean lineage	(from Villeurbanne et Pierre-Bénite)
ZIKA <sup>[2]</sup>	Aedes albopictus
→ ZIKV, flavivirus, isolate SL1602 belong to the Asian lineage	(from Marseille and La Réunion)
DENGUE [1]	Aedes aegypti
→ DENV, flavivirus, isolate of genotype I from Thailand/Laos/New Caledonia and genotype V from Gabon/Haïti	(wild type from Kamphaeng Phet Province/Thailand)

#### MODELING

 $\rightarrow$  An experimental IVD model was built and impleted with R

#### INFERENCE

 $\rightarrow$  Inference was performed with ABC rejection algorithm<sup>[4]</sup>

VS: Healthy Vector VE: Vector in incubation VI: Infectious Vector

VEE : Exposed Vector VEI : Infected Vector VED : Disseminated Vector

#### infected blood

**2)** Freeze-killing at regular intervals of a part of the mosquitoes

**3)** Observation of viruses localisation in mosquitoes

- no viruses : **Exposed**
- body only : Infected
- body+head : Disseminated







- **Differences between IVD** of different virus species.
- Non exponential distribution of durations in the infected state for



### **ZIKV** and **DENV**.

duration (days)

duration (days)

duration (days)

**Figure 1: Estimated distribution of durations in the infected state of the IVD within study mosquitoes for Chikungunya (left), Zika (middle) and Dengue (right) viruses.** Figures were obtained from a part (100) of selected particules (1000) from the model inference (100 000 simulations). Use of infectious doses : 10<sup>6.07</sup> FFU/mL (CHIKV), 10<sup>6.5</sup> FFU/mL (ZIKV), 10<sup>5.81</sup> FFU/mL (DENV).

#### **CONCLUSION AND PERSPECTIVES**

- Assuming exponential distribution of durations to approximate IVD does not always seem relevant.
- Further research of IVD will refine its modeling so that it can be incorporated into vector-borne disease models that contribute to the development of vector-borne diseases management measures.

[1] Fontaine et al. 2018. « Epidemiological Significance of Dengue Virus Genetic Variation in Mosquito Infection Dynamics ». PLOS Pathogens 14 (7): e1007187. https://doi.org/10.1371/journal.ppat.1007187
[2] Lequime et al. 2020. « Modeling Intra-Mosquito Dynamics of Zika Virus and Its Dose-Dependence Confirms the Low Epidemic Potential of Aedes Albopictus ». PLOS Pathogens 16 (12): e1009068. https://doi.org/10.1371/journal.ppat.1009068
[3] Viginier, et al 2022. « Statistical Modeling of Chikungunya Virus Intra-Vector Infection Dynamics in a French Aedes Albopictus Population Reveals an Explosive Epidemic Potential ». medRxiv. https://doi.org/10.1101/2022.11.06.22281997
[4] Sisson S. A., Fan Y., & Beaumont M. 2018. « Handbook of Approximate Bayesian Computation». Chapman and Hall/CRC

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