Unleashing the beast within, unleashing the beast outside

Comparative study of the spreading of a forest arbovirus to anthropized areas and the introduction of a cosmopolitan virus into remote human amazonian populations

Writing and designing a research project
Master 2 Bio-informatics, Université de Paris

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Motivation (1/2)

Decrease of forest cover & increase of anthropization
    → create contact areas (++ edges)
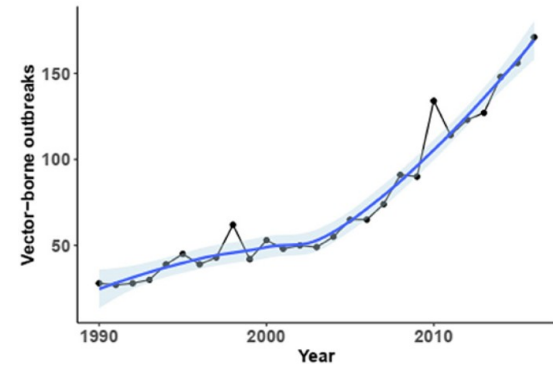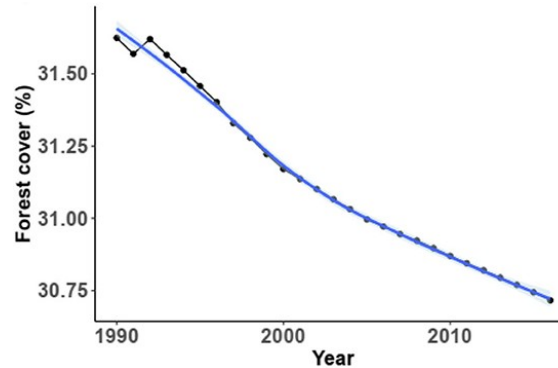   → create micro-climatic conditions at interfence
➡ increase of vector-borne and zoonose diseases

Intensively investigated but many remain to be done :
    - how do pathogens spread ?
    - which species are involved ?

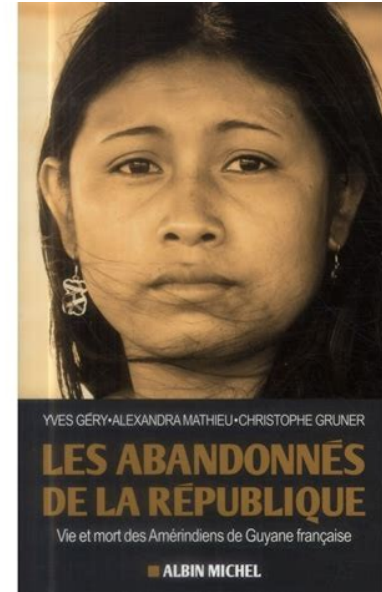Construction of a road,
French Guiana.

Data from *GIDEON* (1996-2016). Morand and Lajaunie, 2021.

Motivation (2/2)

Lots of investigation on tropical diseases from forest to anthropized areas but rarely on the opposite mechanism

vulnerability of isolated populations :

- immunological naivity

- lack of infrastructure and remoteness

- proximity with wild species

- often various chronic diseases

Mathieu, Gery & Gruner. *Les Abandonnés de la République. Vie et morts des amérindiens de Guyane.* (Albin Michel, 2014).

Objectives

• To describe the <u>mechanisms</u> of introduction and spread of two arboviruses in remote areas from urban areas & from forest to anthropized areas.

• To describe <u>dispersal and diversity</u> of recognized and putative vectors, exploring the <u>role of bridge species.</u>

• Identify the <u>genetic determinants</u> of innate immune response of amerindians, Bushi-Nengue and caucasian populations to a ubiquist (Dengue) and a Forest (Mayaro) viruses.

Viruses

Dengue (DENV)
main vector : *A. aegypti*
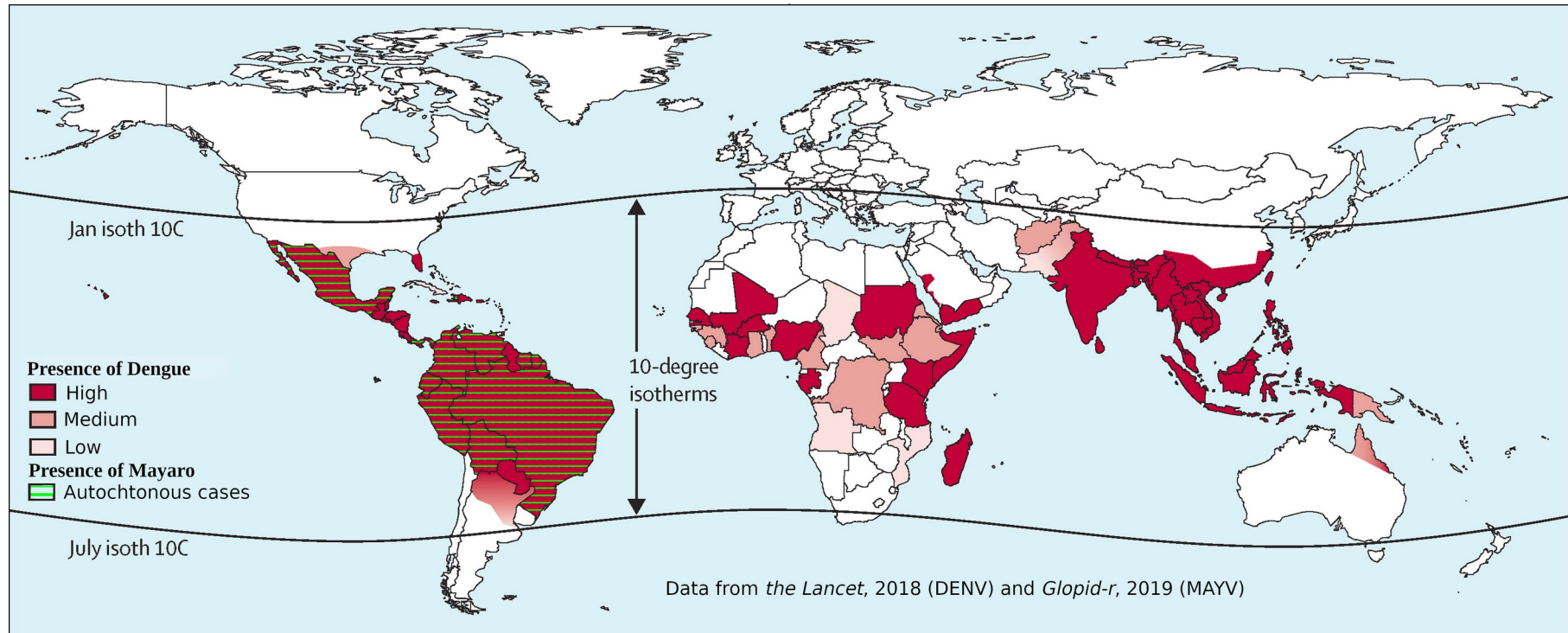most wide-spread mosquito-borne disease
4 serotypes, no crossed immunity

Mayaro (MAYV)
main vector : *Haemogogus* mosquitoes
endemic to humid forests
responsible for several epidemics

Jan isoth 10C

10-degree isotherms

Presence of Dengue
■ High
■ Medium
■ Low
Presence of Mayaro
▦ Autochtonous cases

July isoth 10C

Data from *the Lancet*, 2018 (DENV) and *Glopid-r*, 2019 (MAYV)
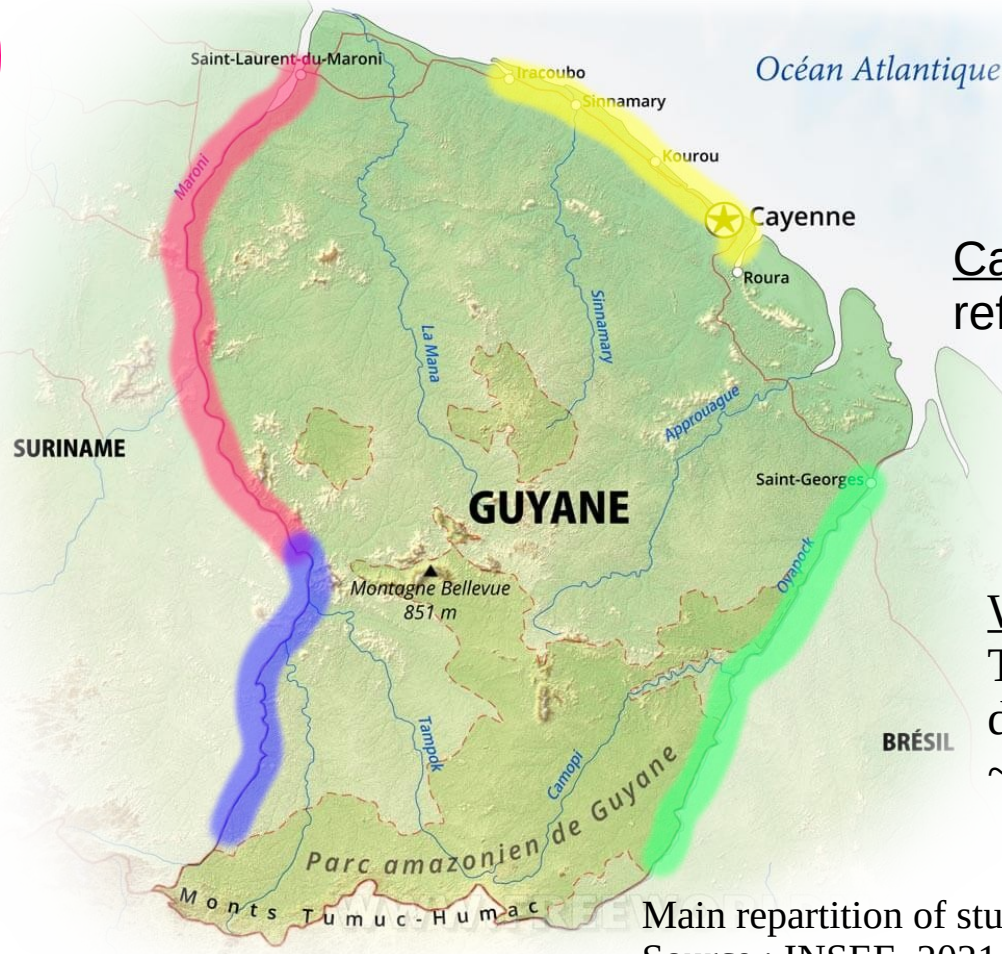
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Populations

<u>Bushi-Nengue</u>
arrived from Africa during
slave-trade
variable population sizes

<u>Wayana</u>
cariban-speaking tribe
most recently arrived
~ 1 500

<u>Caucasians</u> (biological
reference)
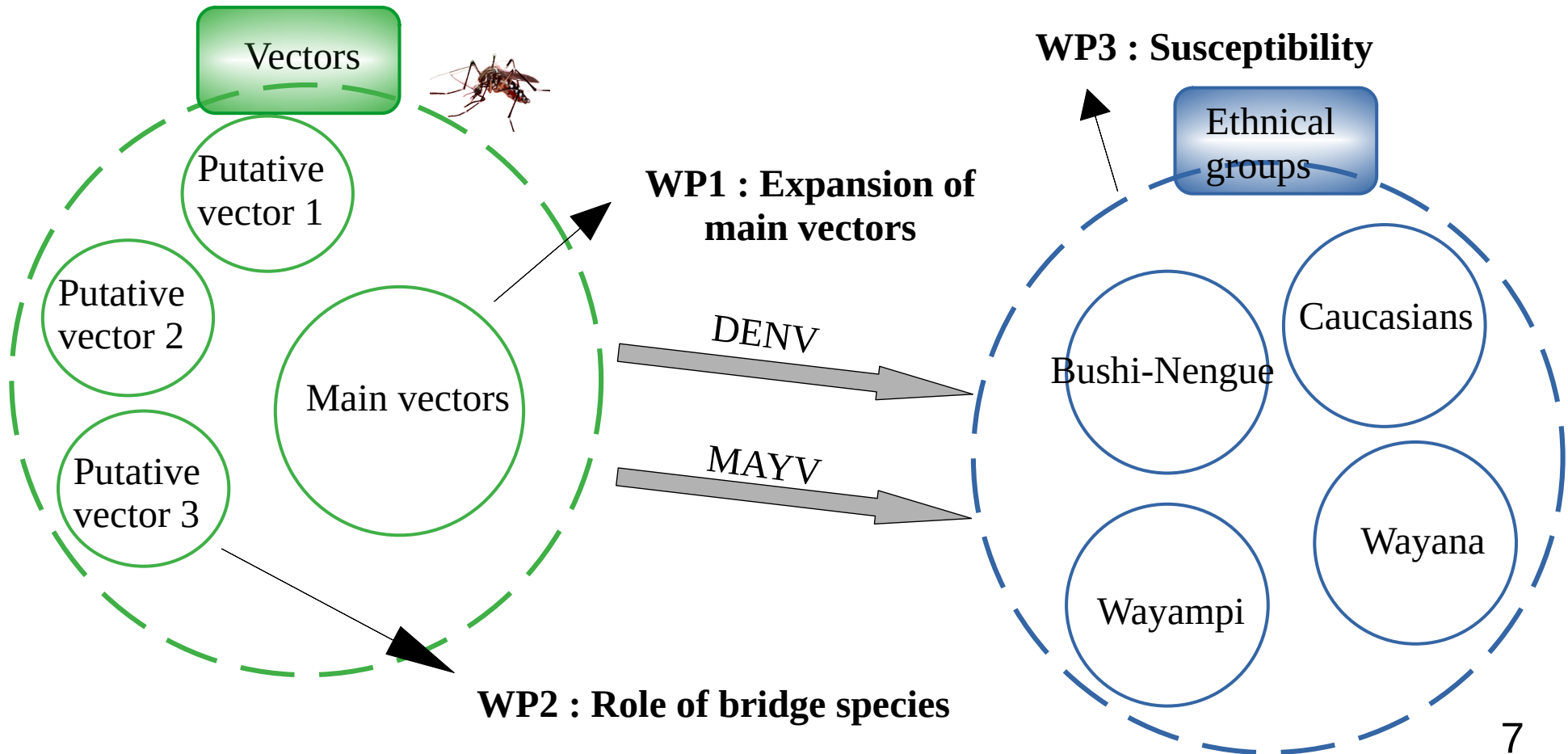

<u>Wayampi</u>
Tupi-guarani
deep Amazon tribe
~ 1 800

Main repartition of studied ethnical groups
Source : INSEE, 2021.

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Overview

WP3 : Susceptibility

Vectors

Putative vector 1

Putative vector 2

Main vectors

Putative vector 3

WP1 : Expansion of main vectors

DENV

MAYV

Ethnical groups

Bushi-Nengue

Caucasians

Wayampi

Wayana

WP2 : Role of bridge species

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WP1. From coast to forest: Ecology and population dynamics of an invader, *Aedes aegypti* mosquitoes

→ *investigate distribution of the main vector of Dengue virus*

Task 1. Mosquitoes sampling

field work, using bated passsive box traps
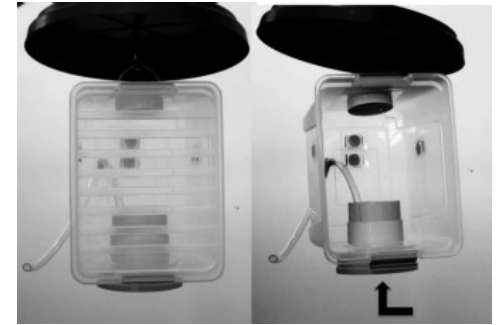
Task 2. Population genomics

double-digest Restriction site-Associated DNA (ddRAD) protocol

→ panel of SNPs

demographic history & geographical structuring of genetic variation linked with disturbance gradient

Task 3. Dengue vector spreading

detection of previous Dengue virus infections

Box traps. Ritchie et al., *Journal of Medical Entomology*, 2013

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WP2. Escaping from forests : searching for cryptic vectors, carrying cryptic viruses

→ *investigate existence of bridge vectors and others viruses*

Task 1. Identification of mosquitoes communities
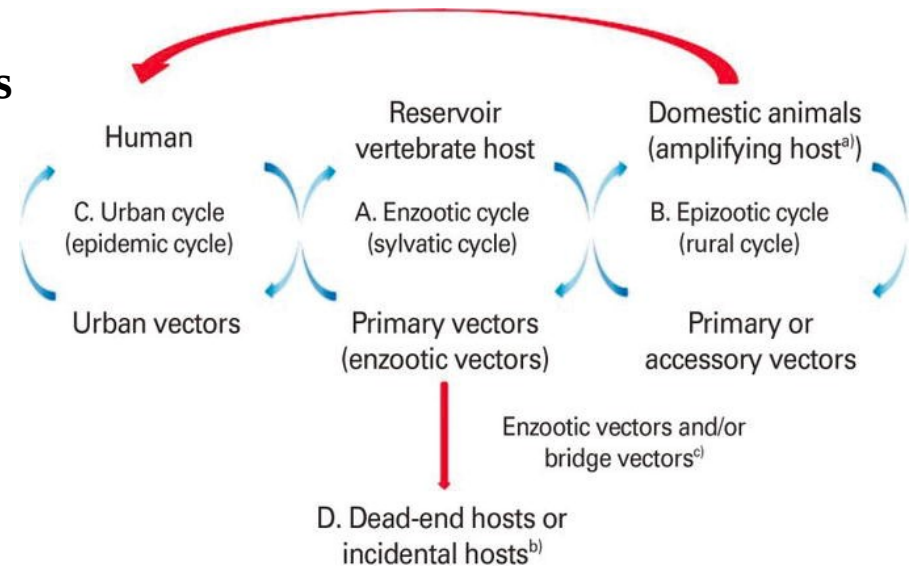
metabarcoding using reference librairies

Task 2. Identification of viral diversities

high-throughput shotgun sequencing

→ metatranscriptomics analysis

Task 3. Network analysis

ecological network tools (innovative purpose)

Role of bridge vectors. Go and Balasuriya, *Clinical and Experimental Vaccine Research*, 2014.

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WP3. Immuno-genetics for severe infections : an ethnic approach of the risk

→ *ethnical drive on innate immune response*

Task 1. Sampling

saliva (SNP typing) & blood (PBMC) : 50 people from each group

Task 2. Genotyping and serology

whole-genome genotyped (Illumina®), analyze of Haplotypes

determination of serological status (previous exposures to arborviruses)

Task 3. BMC simulation and severe Dengue

comparison unstimulated and stimulation with DENV and MAYV

≠ expression of I IFNs, ISGs and cytokine using RT-qPCR

≠ expression levels (RNA) using Illumina HiSeq2000

- associations between SNPs and gene expression (expression Quantitative Trait Loci)

Expected difficulties & fall-back solutions

- All considerations will be taken regarding the use of ethnical information, according to the recommandations of the Comité Consultatif National d'Éthique.

- Respect of "Access and Benefits Sharing" of genetic ressources

- Parts of the work will be implemented in the National Park, sampling mosquitoes will require adhoc authorizations.

- Respect of the traditional cultures, approval of tribal chiefs.

- Retranscription and explanation of the study to the communities concerned.

Scientists meeting community representatives in Camopi village, 2018.

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Schedule & costs

	Trimesters T3_2022	T4_2022	T1_2023	T2_2023	T3_2023	T4_2023	T1_2024	T2_2024
KickOff Meeting & meetings with local & communities authorities	■							
Analysis & publications						■	■	■
WP1								
Task 1. Mosquitoes sampling	■		■					
Task 2. Population genomics					■	■		
Task 3. Dengue vector spreading		■		■				
WP2								
Task 1. Metabarcoding		■		■				
Task 2. Metatranscriptomics			■		■			
Task 3. Network analysis						■		
WP3								
Task 1. sampling		■	■	■				
Task 2. Genoyping and serology					■	■		
Task 3. BMC simulation						■		

WP1	42 200 €
WP2	38 000 €
WP3	107 500 €
Transversal costs	486 345 €
Totals Total projet	674 045 €
Total requested	366 845 €

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Outcomes

- Anticipation of the spread of vectors along perturbation gradients

- Surveillance tools and workflow for zoonose and vector-borne diseases emergence

- If conclusive results, initiate communties-based approaches of treatments
  - consider ethnical uniqueness to adress conditions
  - less intrusive than presonalized medecine

Thank you for your attention.

Traditional *Tukusipan*, Taluen, Wayana village.