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*Assessing virus circulation levels in the context of high serological cross-reactivity: the case of Mayaro and Chikungunya virus*

Mayaro virus (MAYV) is often cited as a likely candidate for the next major arbovirus emergence and quantifying its circulation in human populations in the Americas is therefore important to inform risk assessments. However, this task is difficult because MAYV symptoms are mostly unspecific and serology is challenging to interpret because of the large chikungunya virus (CHIKV) outbreak that occurred in 2014-2015 and high cross-reactivity between MAYV and CHIKV. This problem of cross-reactivity hampers serological studies across many different pathogens.

Here we demonstrate that by jointly analyzing serological results alongside data on the age and location of participants, we can simultaneously reconstruct the history of circulation of the viruses and the extent of cross-reactivity. We applied our approach to serological results of 2,697 individuals from across French Guiana obtained with a multiplexed immunoassay that returned a relative fluorescence intensity (RFI) for each pathogen.

We quantify the impact of cross-reactivity on the RFI for the infecting and non-infecting virus. We find evidence of regular MAYV spillovers, with male adults particularly affected and seroprevalence in forested regions as high as 10