

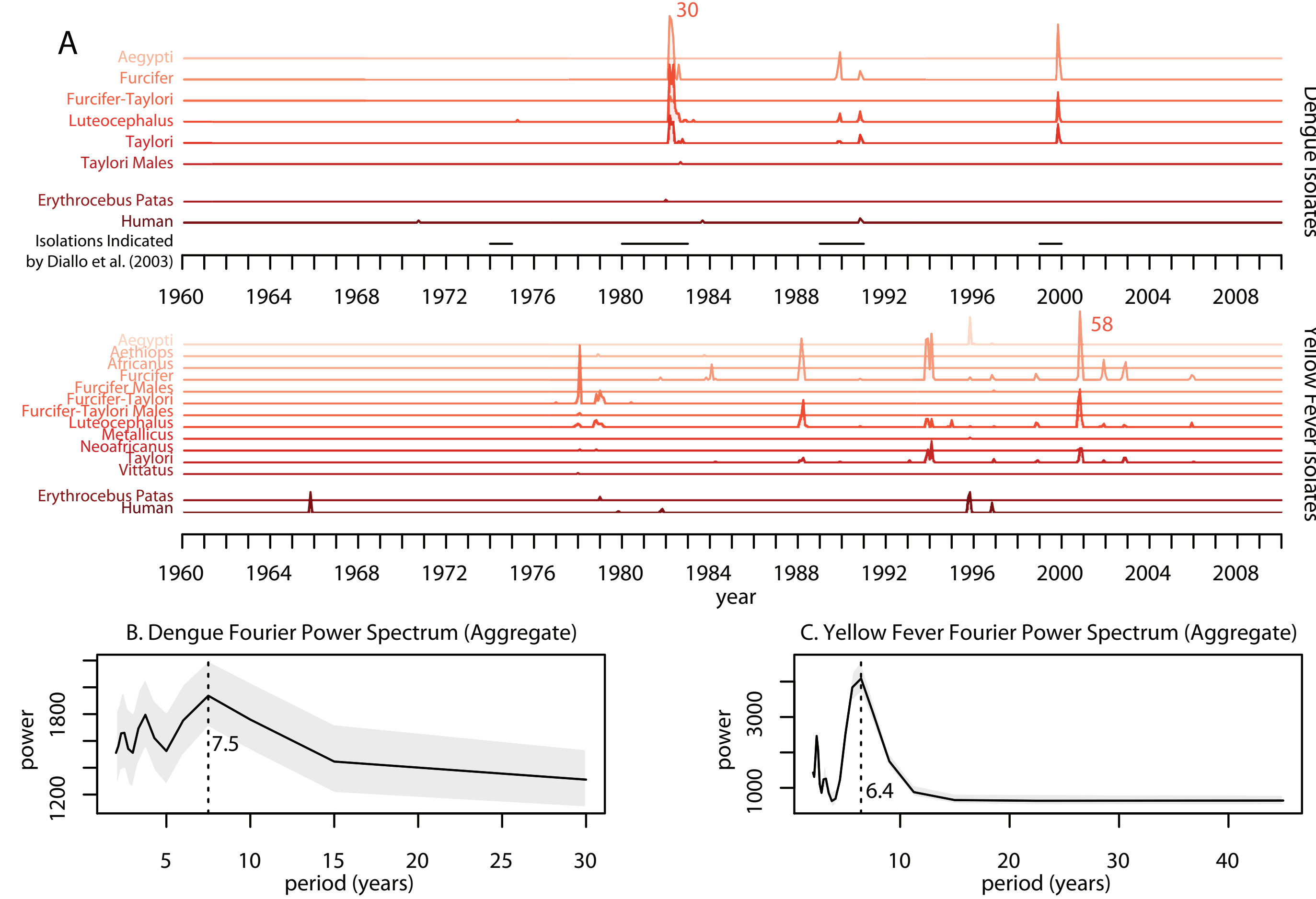
# A Multi-host, Multi-vector SIR Model of Dengue Virus Transmission in Senegal

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## Introduction

Dengue virus is transmitted in two distinct transmission cycles; transmission among non-human primates by *Aedes* mosquitoes in the forest canopy (the sylvatic cycle) and transmission among humans by *Aedes aegypti* in an urban cycle (the endemic cycle). These cycles are usually thought to be non-overlapping. While there is evidence to suggest maintenance of transmission exclusively among non-human primates in Western Africa and Malaysia, with occasional spillover to humans, the precise role of particular primates including humans in the dengue transmission cycle is unknown. [Diallo 2003, Vasilakis & Weaver 2008, Rudnick 1967] Here we use a mathematical model to investigate the transmission dynamics of dengue among multiple primate hosts, including humans. We investigate the impact of differential birth and death rates, transmission probabilities and coupling rates between host species on temporal dynamics of incidence of dengue virus infection.



**Figure 1 Summary of Dengue and Yellow Fever Isolates, 1962 -- 2007** Panel A shows number of dengue and yellow fever virus isolates over time separated by species. Short horizontal bars indicate sylvatic isolations reported in Diallo et al. (2003). Numbers indicate maximum values for each virus isolates to give a sense of scale. Yellow fever is included to show that periods of non-activity in the dengue time series is not due to a lack of collection activities. Panel B shows the Fourier power spectrum with 95% bootstrap confidence intervals for the aggregated dengue isolates; and panel C shows the Fourier power spectrum with 95% bootstrap confidence intervals for the aggregated yellow fever isolates (note the difference of scale from panel B).

## Model

Our frequency dependent SIR model with  $j$  mosquito species and  $i$  primate species extends a framework presented in Keeling and Rohani (2008). The model equations are as follows, where  $S$ ,  $I$  and  $R$  denote the susceptible, infectious and recovered classes of each species:

$$\begin{aligned} S'_{m_j}(t) &= \mu_{m_j} N_{m_j}(t) - \sum_i r_{m_j, p_i} \beta_{p_i, m_j}(t) I_{p_i}(t) S_{m_j}(t) / N(t) - v_{m_j} S_{m_j}(t) \\ I'_{m_j}(t) &= \sum_i r_{m_j, p_i} \beta_{p_i, m_j}(t) I_{p_i}(t) S_{m_j}(t) / N(t) - v_{m_j} I_{m_j}(t) \\ S'_{p_i}(t) &= \mu_{p_i} N_{p_i}(t) - \sum_j r_{m_j, p_i} \beta_{m_j, p_i}(t) I_{m_j}(t) S_{p_i}(t) / N(t) - v_{p_i} S_{p_i}(t) \\ I'_{p_i}(t) &= \sum_j r_{m_j, p_i} \beta_{m_j, p_i}(t) I_{m_j}(t) S_{p_i}(t) / N(t) - v_{p_i} I_{p_i}(t) \\ R'_{p_i}(t) &= v_{p_i} I_{p_i}(t) - v_{p_i} R_{p_i}(t) \\ \beta_{p_i, m_j}(t) &= b_{p_i, m_j} [1 + c_j \cdot \cos(t 2\pi / 365)] \\ \beta_{m_j, p_i}(t) &= b_{m_j, p_i} [1 + c_j \cdot \cos(t 2\pi / 365)] \\ N_{m_j} &= S_{m_j} + I_{m_j} \\ N(t) &= \sum_i S_{p_i}(t) + I_{p_i}(t) + R_{p_i}(t) \end{aligned}$$

For each primate-mosquito subsystem, we assume that each primate has a vector species (or this could represent distinct populations within a species) that is the primary source of bites that could transmit dengue. We can represent the different biting rates as a matrix  $R$ :

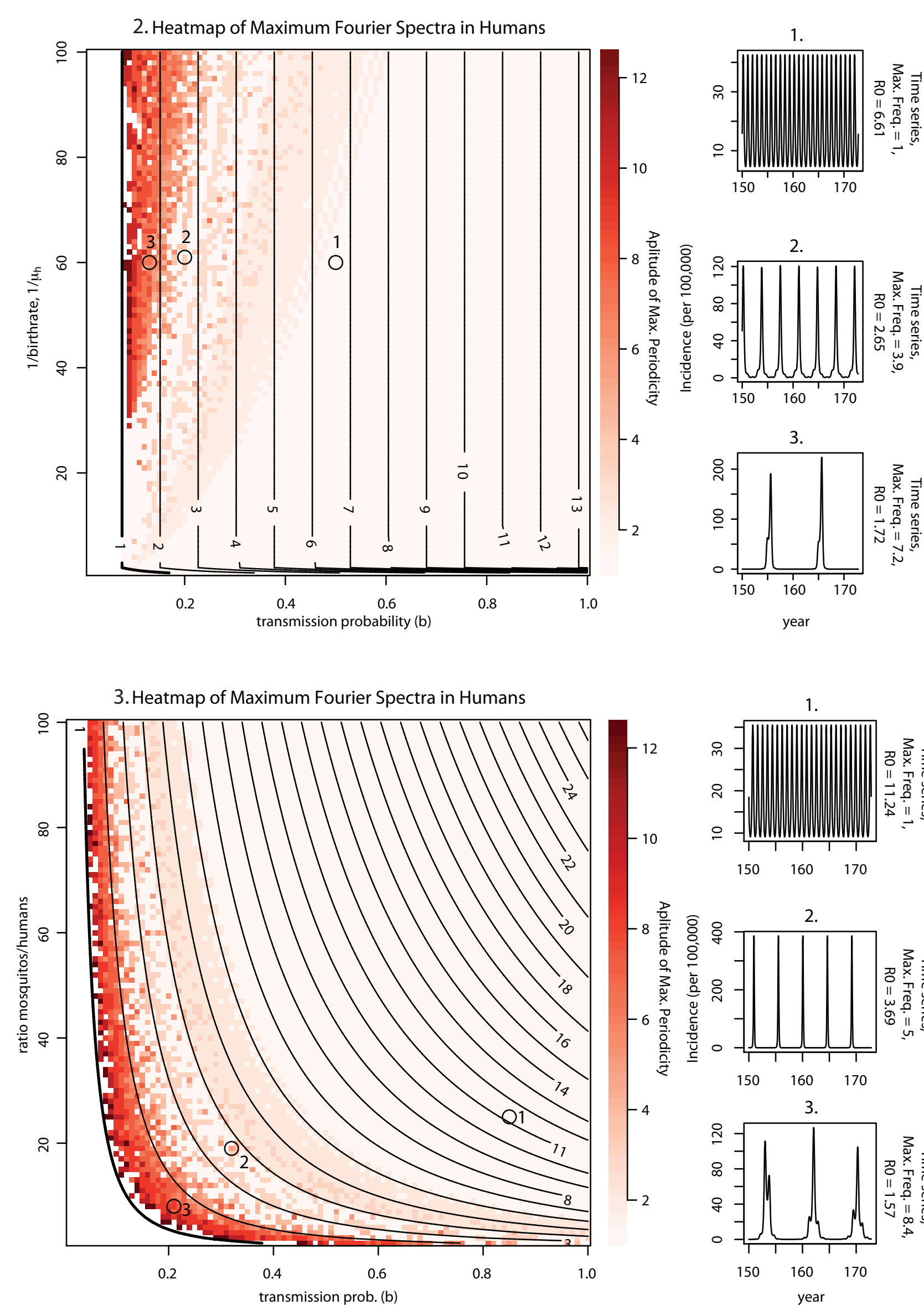
$$R = \begin{pmatrix} r_{p_1, m_1} & r_{p_2, m_1} & \dots & r_{p_i, m_1} & \dots \\ r_{p_1, m_2} & r_{p_2, m_2} & \dots & r_{p_i, m_2} & \dots \\ \vdots & \vdots & \ddots & \vdots & \ddots \\ r_{p_1, m_j} & r_{p_2, m_j} & \dots & r_{p_i, m_j} & \dots \end{pmatrix}$$

Baseline parameters are:

$$\begin{aligned} 1/\mu_h &= 60, 1/\mu_p = 15, 1/\gamma_h = 1/\gamma_p = 4, \\ b_{hm_1} &= b_{hm_h} = b_{pm_2} = b_{mp} = 0.3, \\ c_j &= 0.05, r_{m_1, h} = r_{m_2, p} = 0.5, \text{ and } N_{m_j} = 25000. \end{aligned}$$

## Single Host, Single Vector

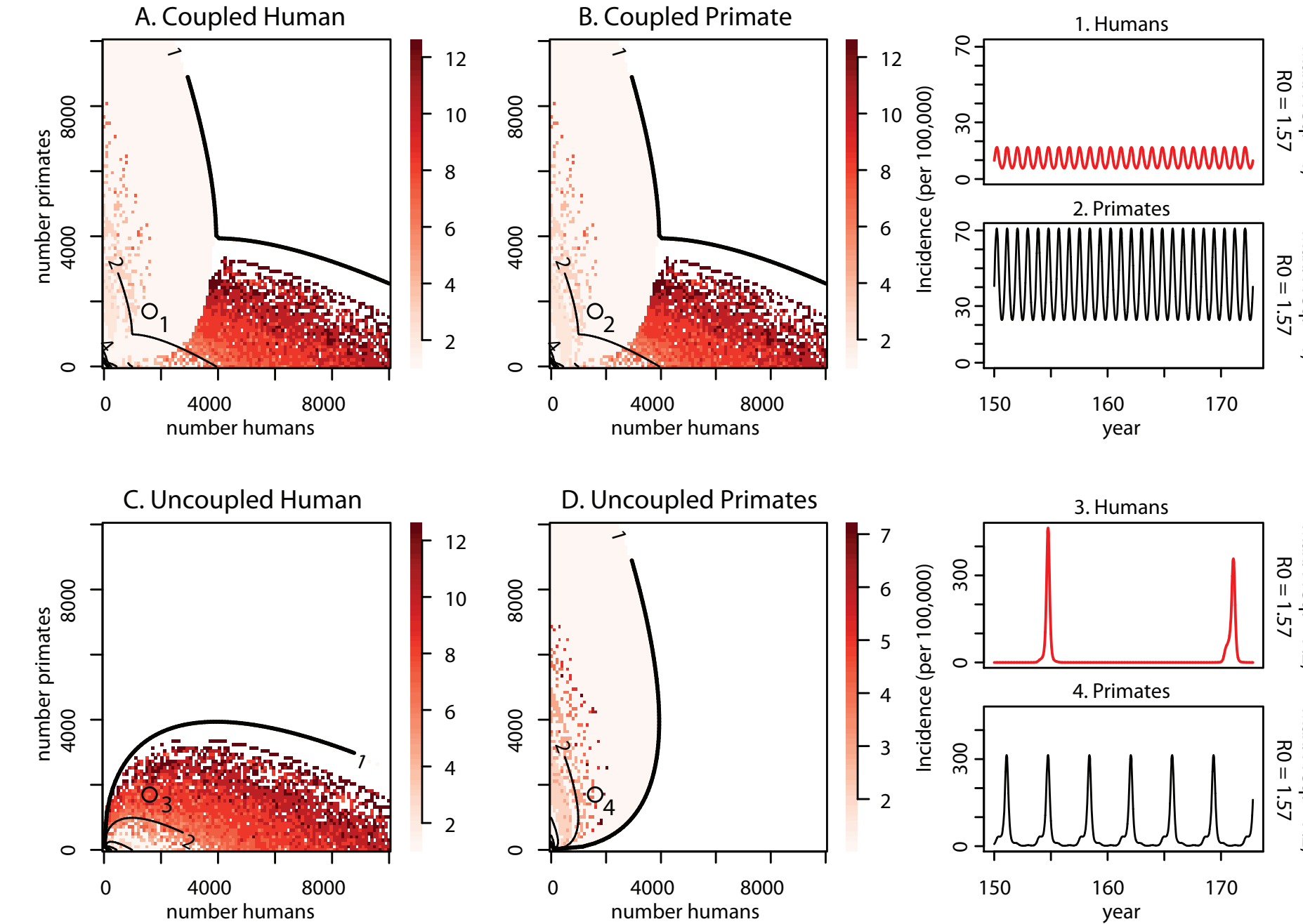
Multi-annual cycles are found in the single host, single vector case when transmission probabilities and average daily biting rates are low and all other parameters are within reasonable values as suggested by the literature.



**Figures 2 & 3 Effect of Demographics and Transmission Probabilities on Single Host, Single Vector Model Dynamics** Heat maps of period of maximum Fourier spectra peak with corresponding example epidemic time series of incidence (per 100,000). Figure 2 compares transmission probabilities (x-axis) and 1/birth rate (y-axis), figure 3 compares transmission probabilities (x-axis) and duration of infection (1/recovery rate) (y-axis). Circles indicate example time series on right.

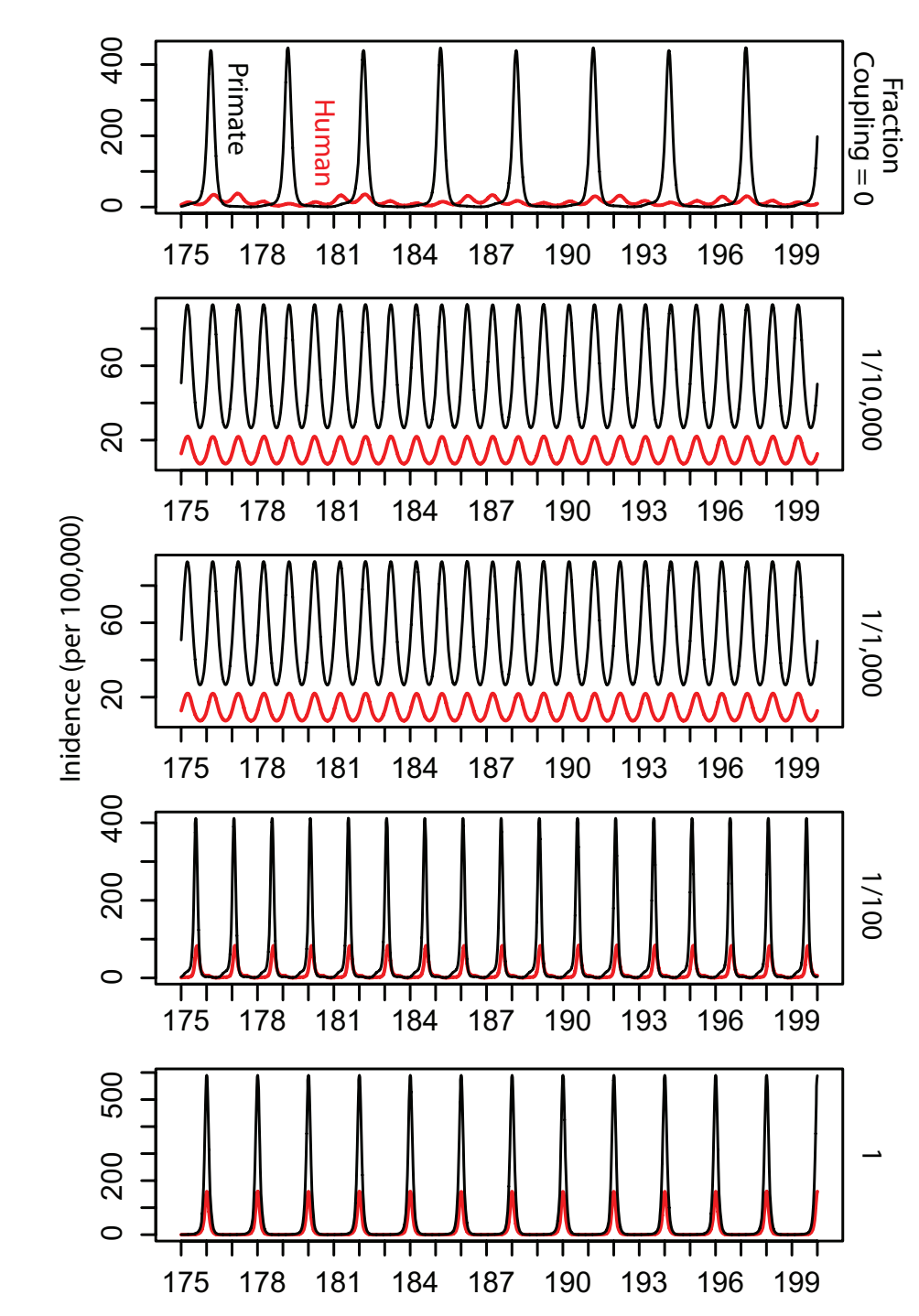
## Two Host, Two Vector

Numbers of Humans and Primates

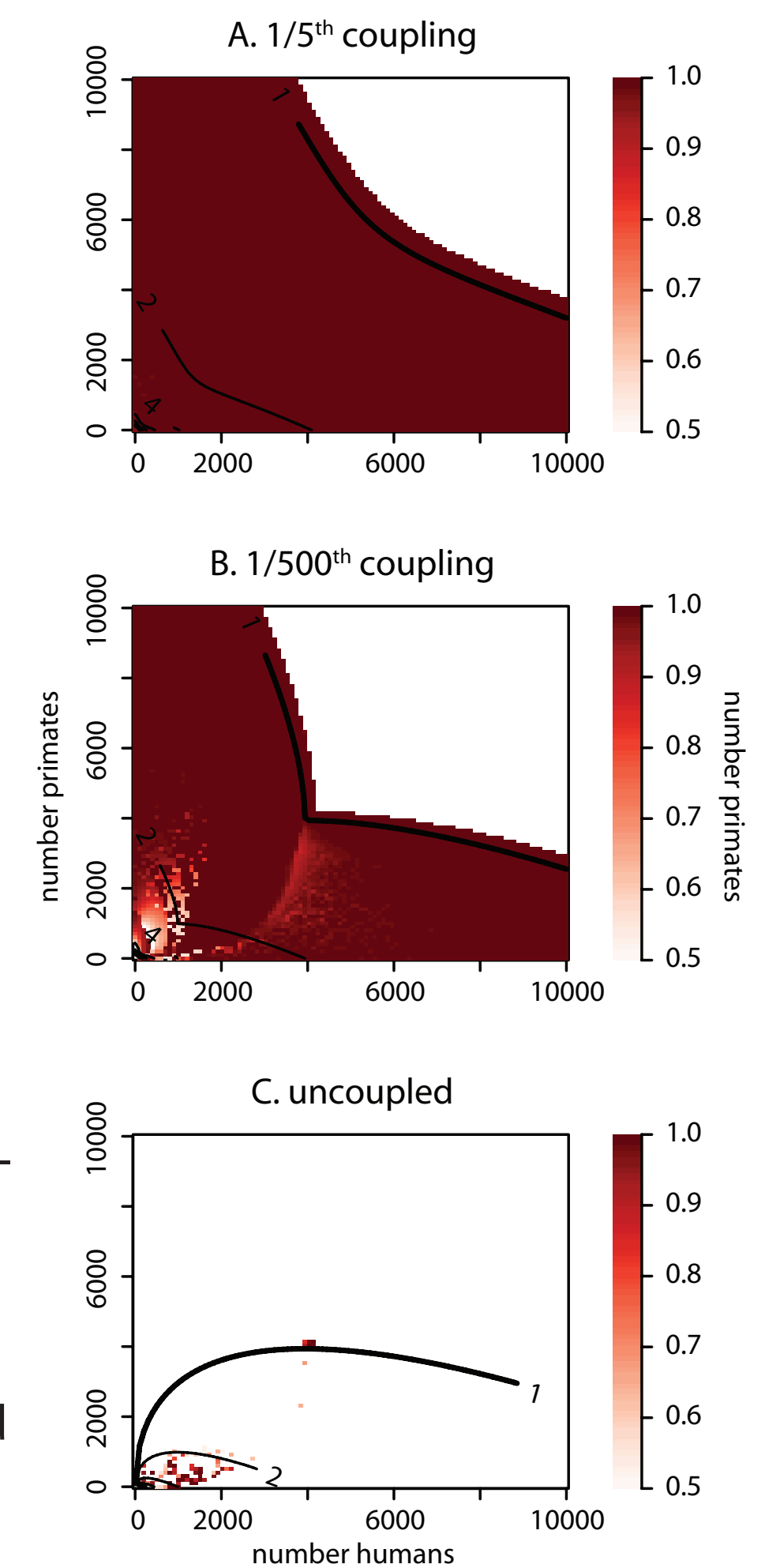


**Figure 4 Incidence in Humans and Primates in the Coupled and Uncoupled Systems** Top panels (A's and B's) are coupled at 1/500th of the on-diagonal biting rates. Bottom panels (C's and D's) are uncoupled. Note the dominance of the higher birth rate primate on the period of oscillations in the coupled simulations. This indicates that the higher birth rate species determines the period of epidemic oscillation only when its  $R_0$  is greater than one.

## Coupling



**Figure 5 Example Time Series with Increasing Coupling** This figure shows the effect of increasing coupling rates from a base biting rate of  $r_{m_1, h} = r_{m_2, p} = 0.5$ , with other parameters were held fixed. Baseline parameters as in Figure 4.



**Figure 6 Increasing Coupling Shows Increasing Correlation** Heat maps of correlation coefficient between human and primate species. All panels show number of primates on the y-axis and numbers of humans on the x-axis. Panel A, B and C show levels of coupling at 1/5<sup>th</sup>, 1/500<sup>th</sup> and 1/1 of baseline biting rates.

## Conclusions

We find long-period oscillations in single host single vector systems when the force of infection - both the transmission probabilities,  $b$ , and biting rates,  $r$  - are low, and other parameters are within a reasonable range suggested by the literature.

We model coupling by adding additional host-vector systems and find that with even modest amounts of coupling between the various host-vector systems, epidemics synchronize and all species experience peaks in incidence concurrently. This is consistent with the small number of dengue virus isolates collected over the last 40 years across several mosquito and primate species from Senegal (see Figure 1). We notice that under epidemic synchrony the species with the highest birth rate drives the epidemic dynamics in regions where its value of  $R_0$  is greater than one. To be consistent with the observed data and the allometric scaling of biting and birth rates we draw the conclusion that a smaller species with higher birth rate has a smaller probability of transmission (and therefore force of infection) than a larger species with a lower birth rate. If this was not the case, higher frequency and unsynchronized isolations would be seen.

### Acknowledgements

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