Assessing the threat of establishing a sylvatic Zika virus cycle in South America

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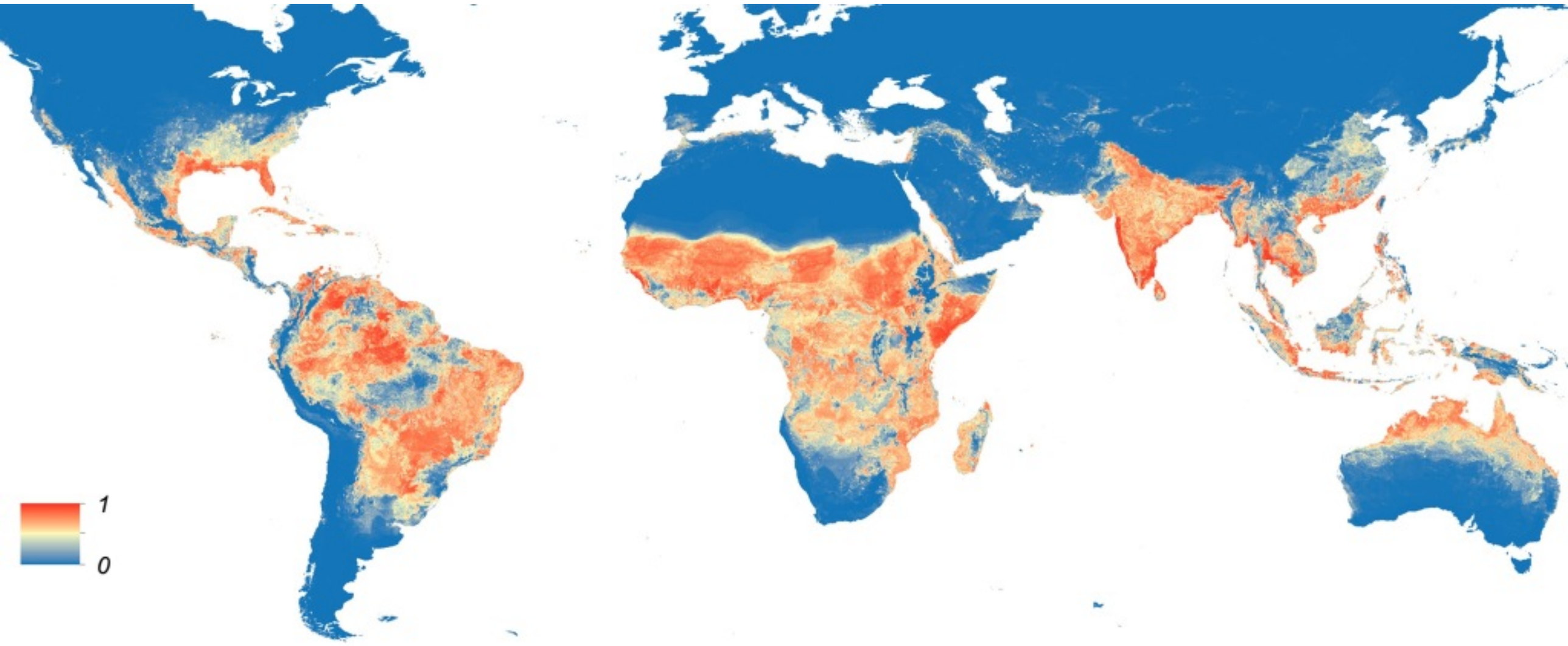
How likely is it that Zika virus will establish a sylvatic cycle in South America?



Kraemer et al., 2015, eLife

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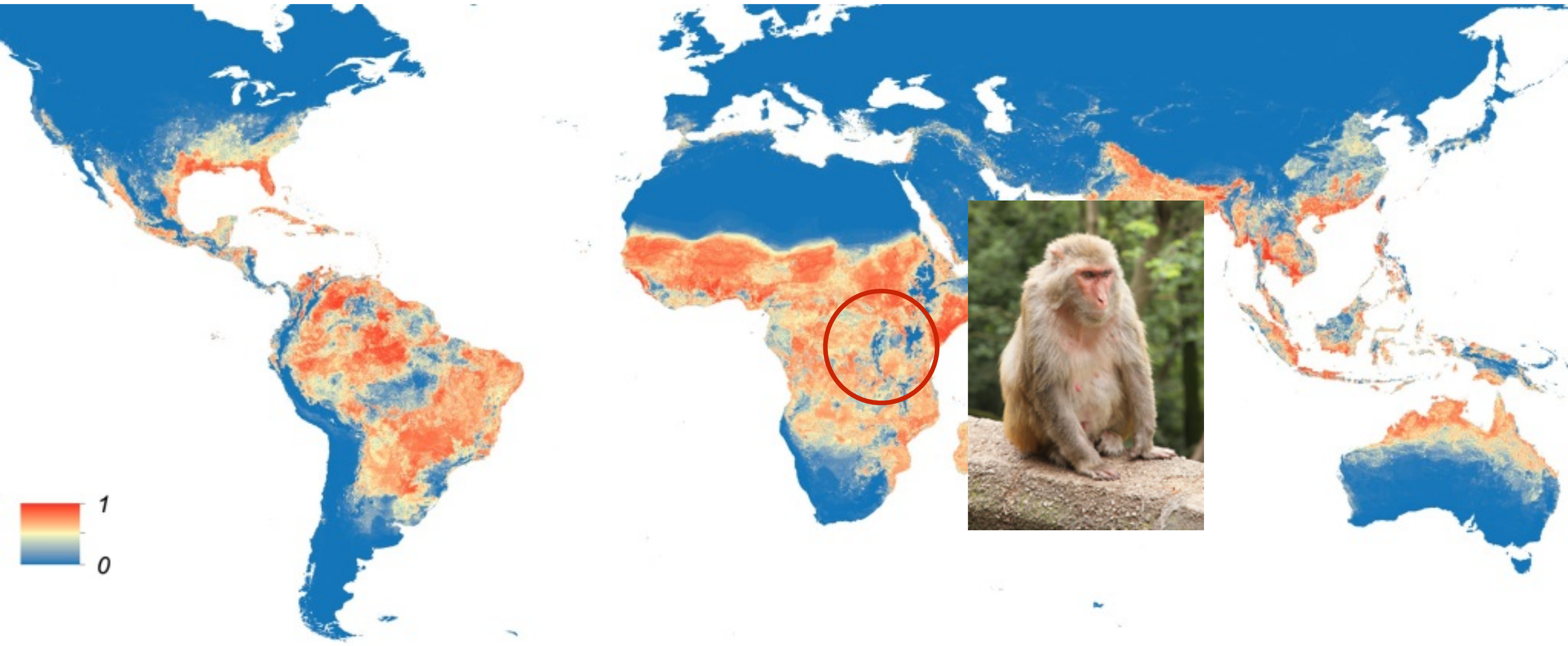

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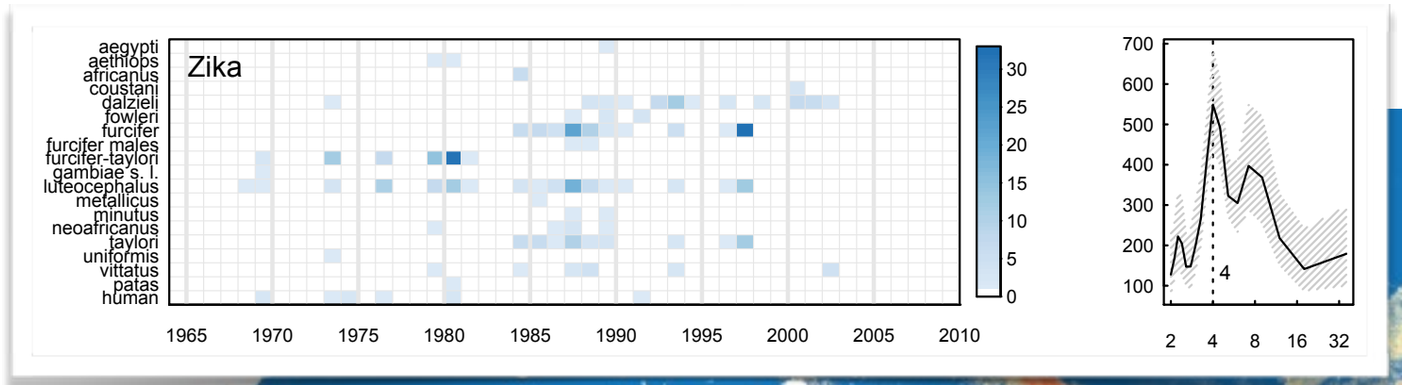

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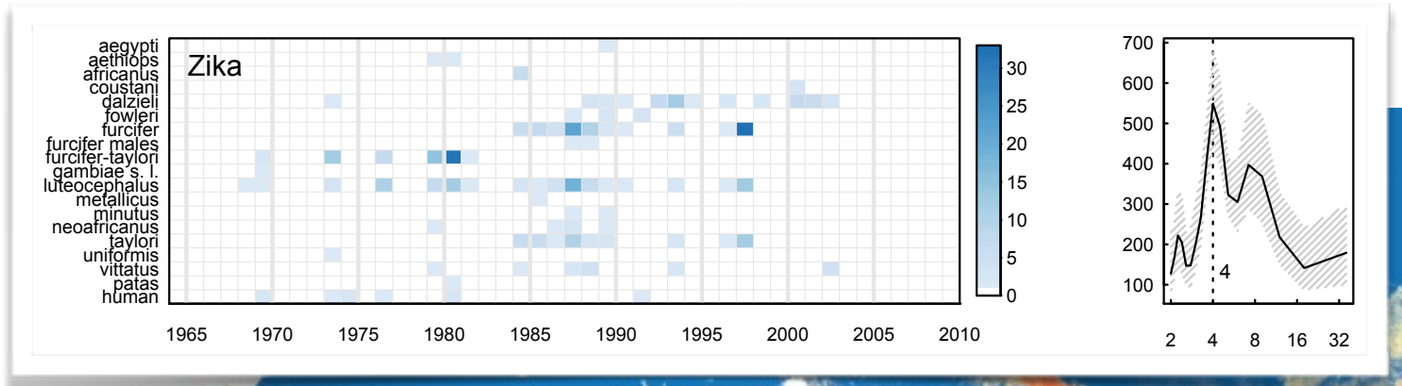

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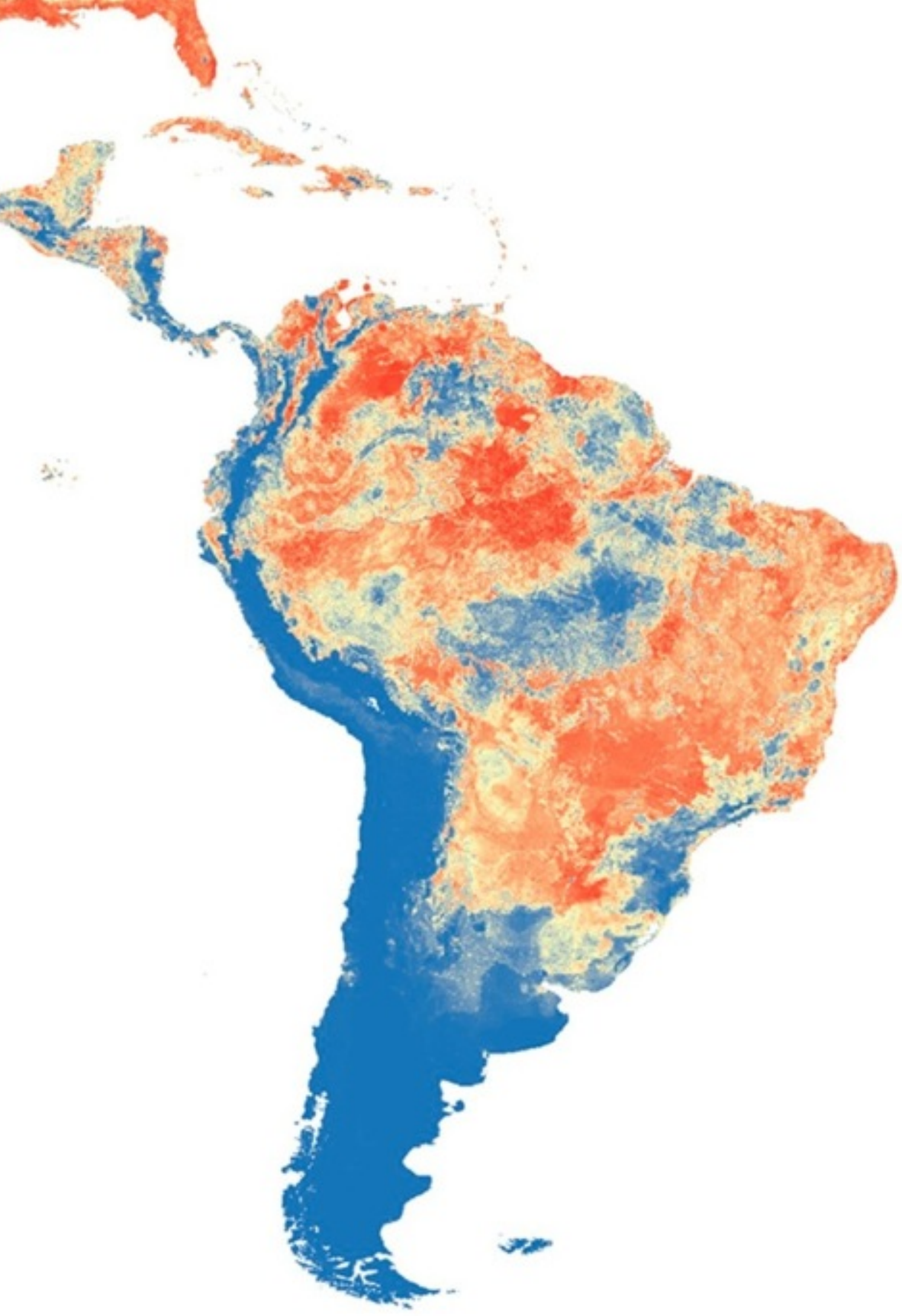
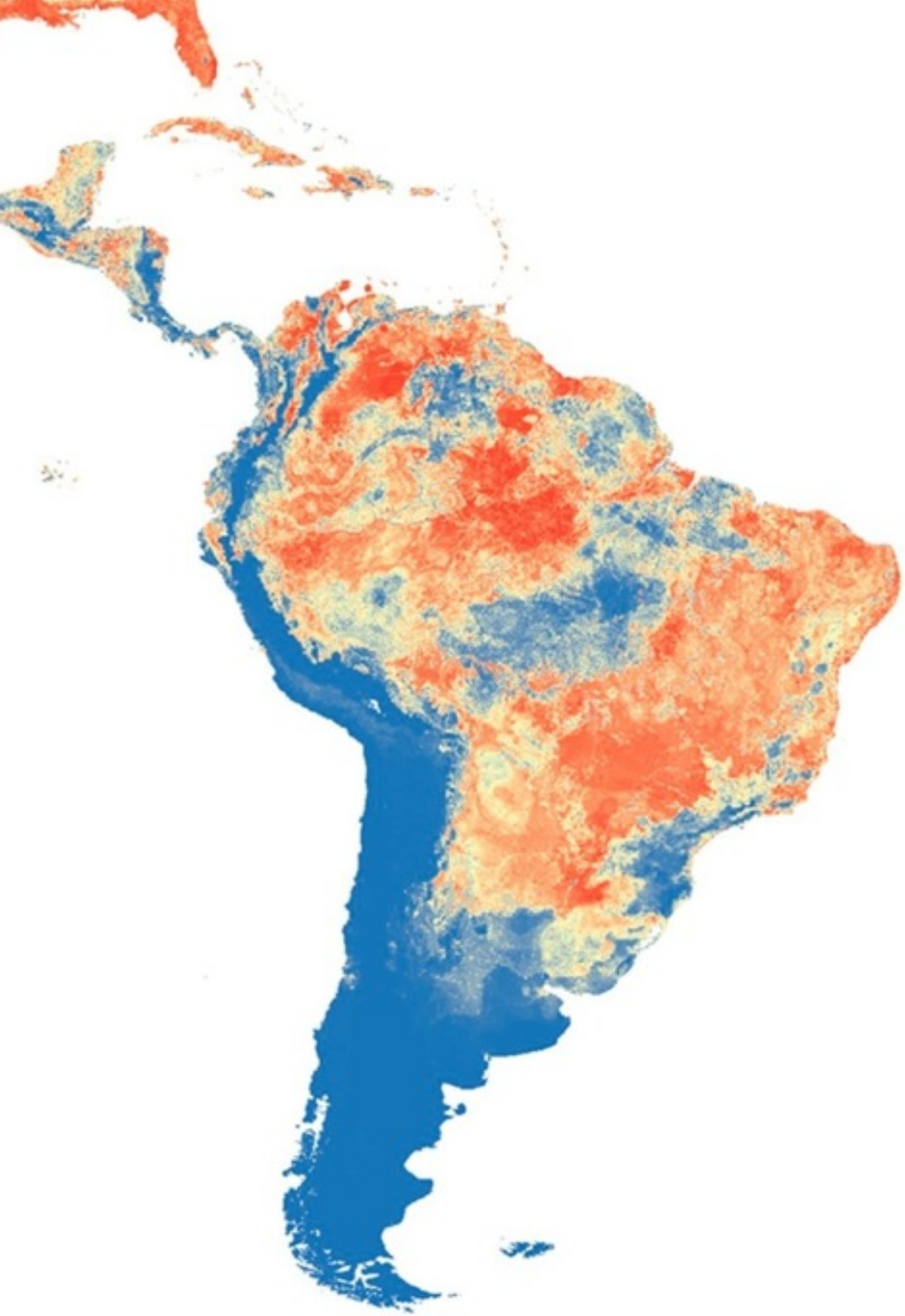
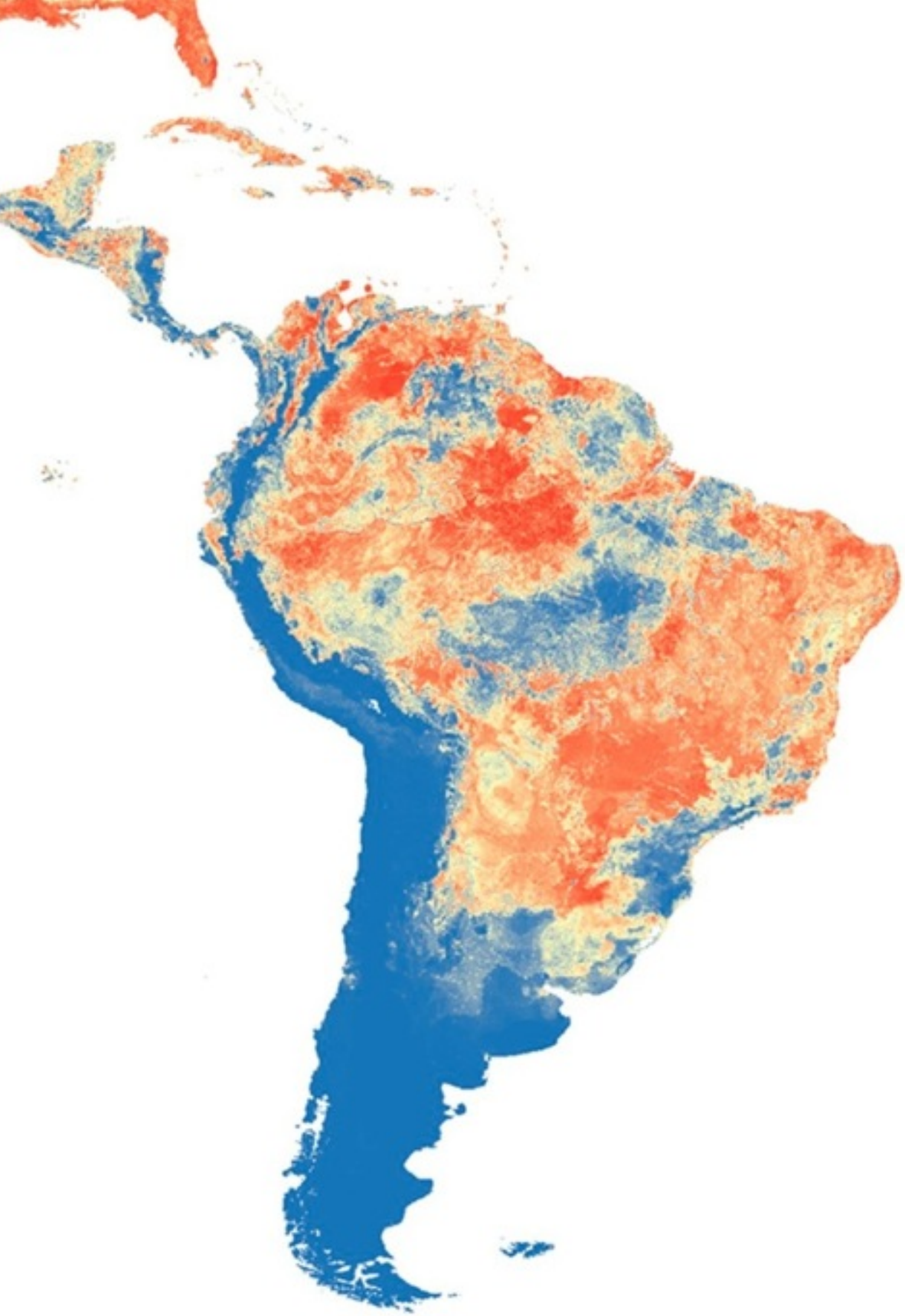
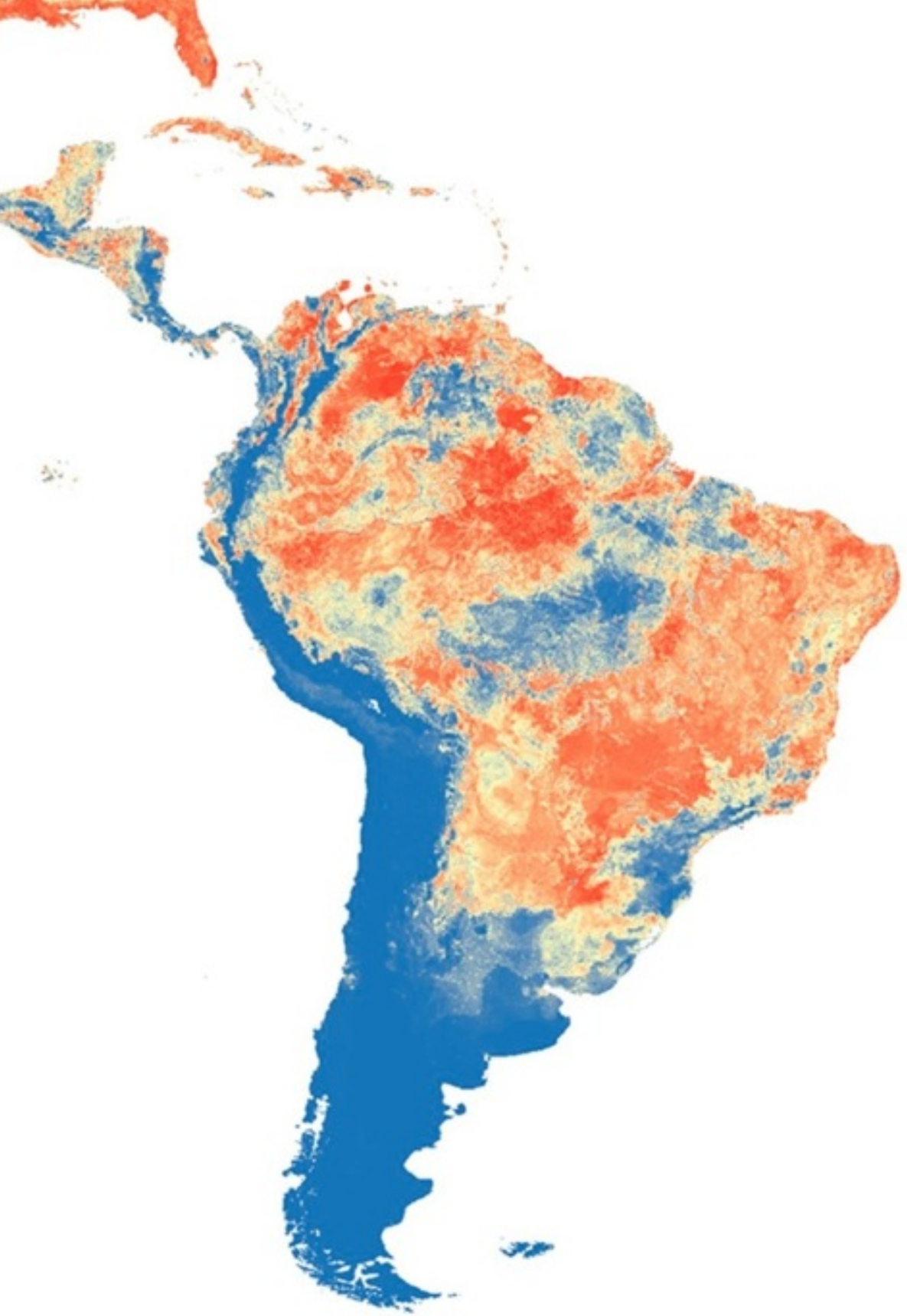




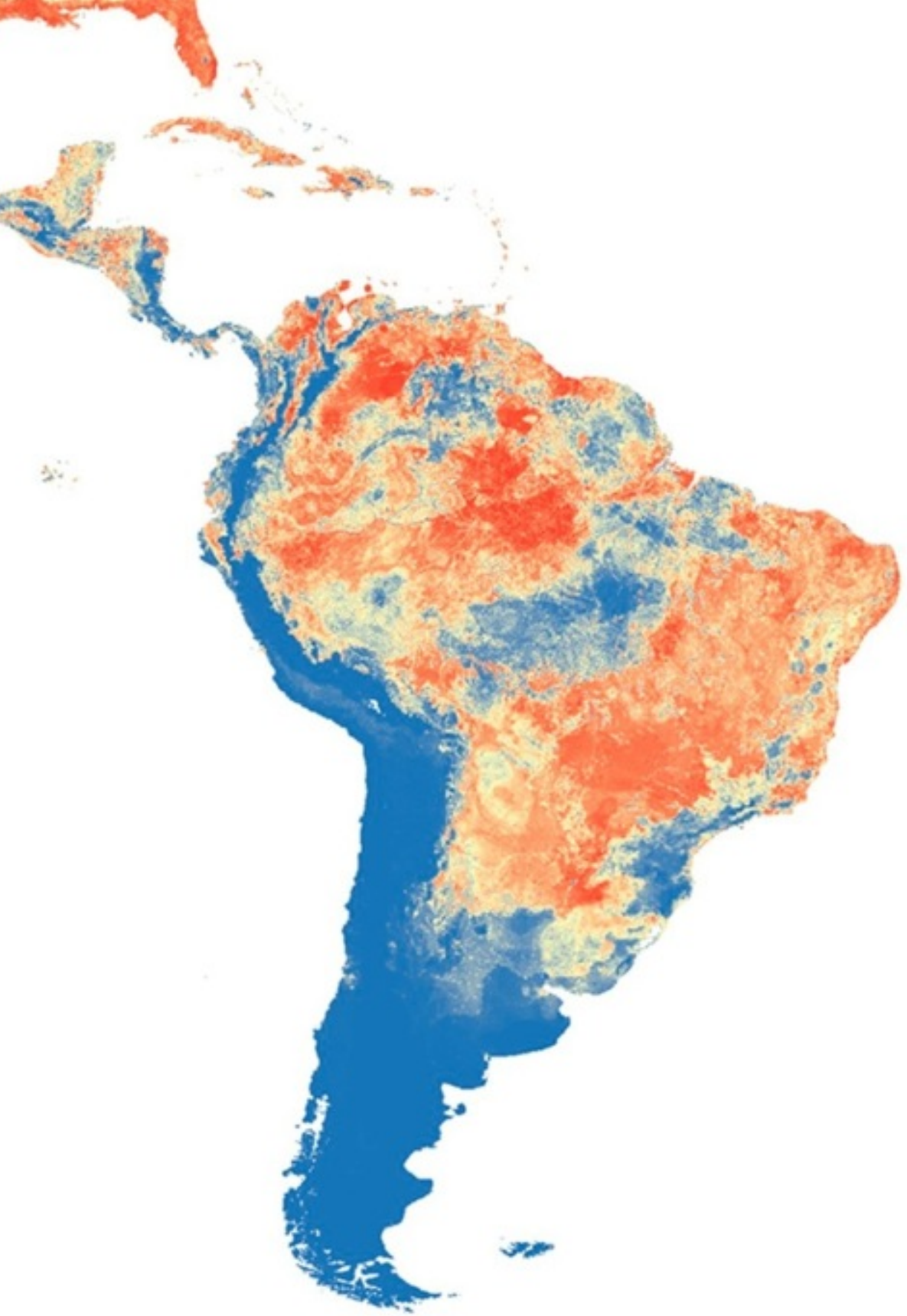
1. What is a sylvatic cycle?



1. What is a sylvatic cycle?
2. Why would we think it is possible?



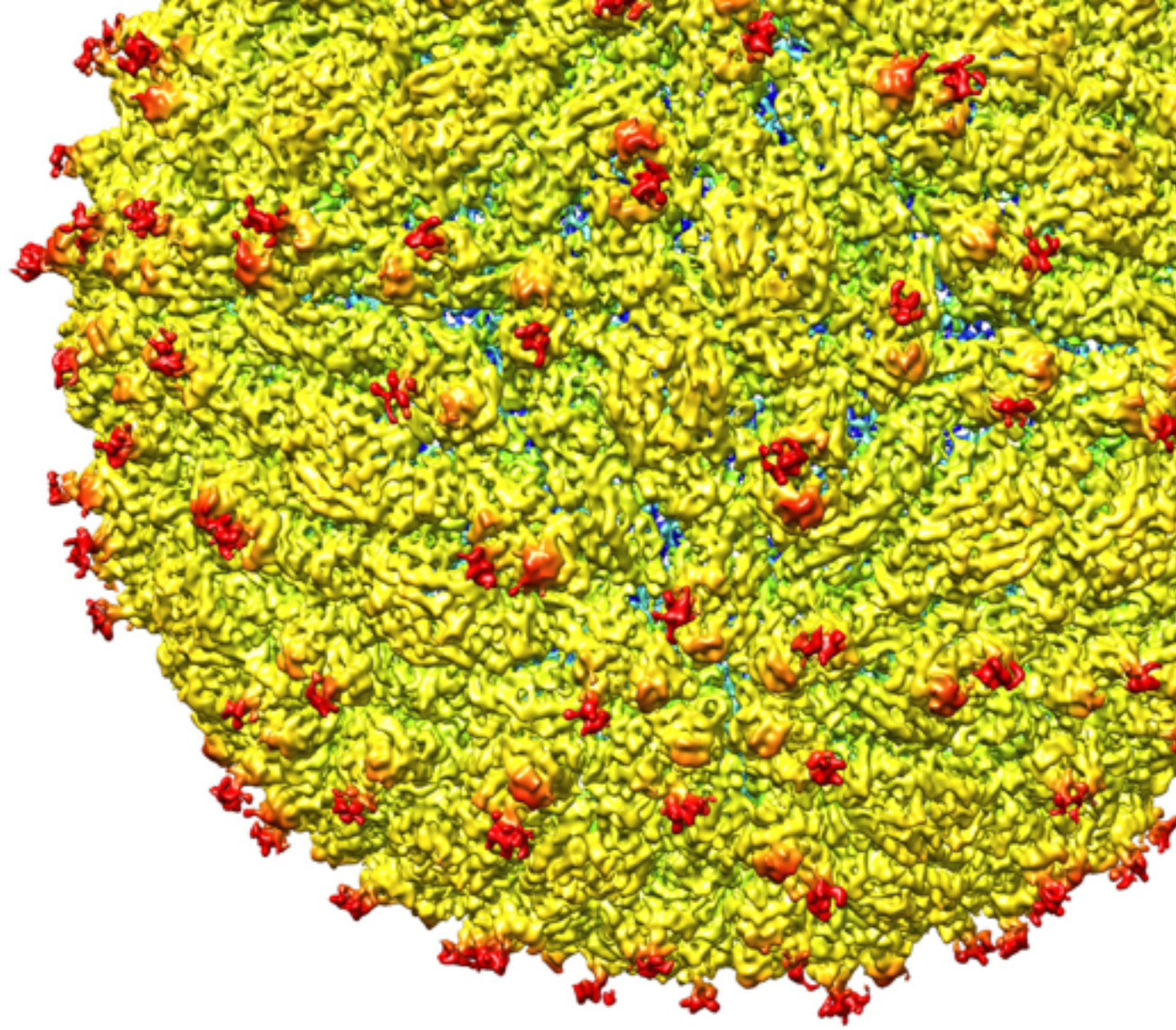
1. What is a sylvatic cycle?
2. Why would we think it is possible?
3. What is the probability of establishment?



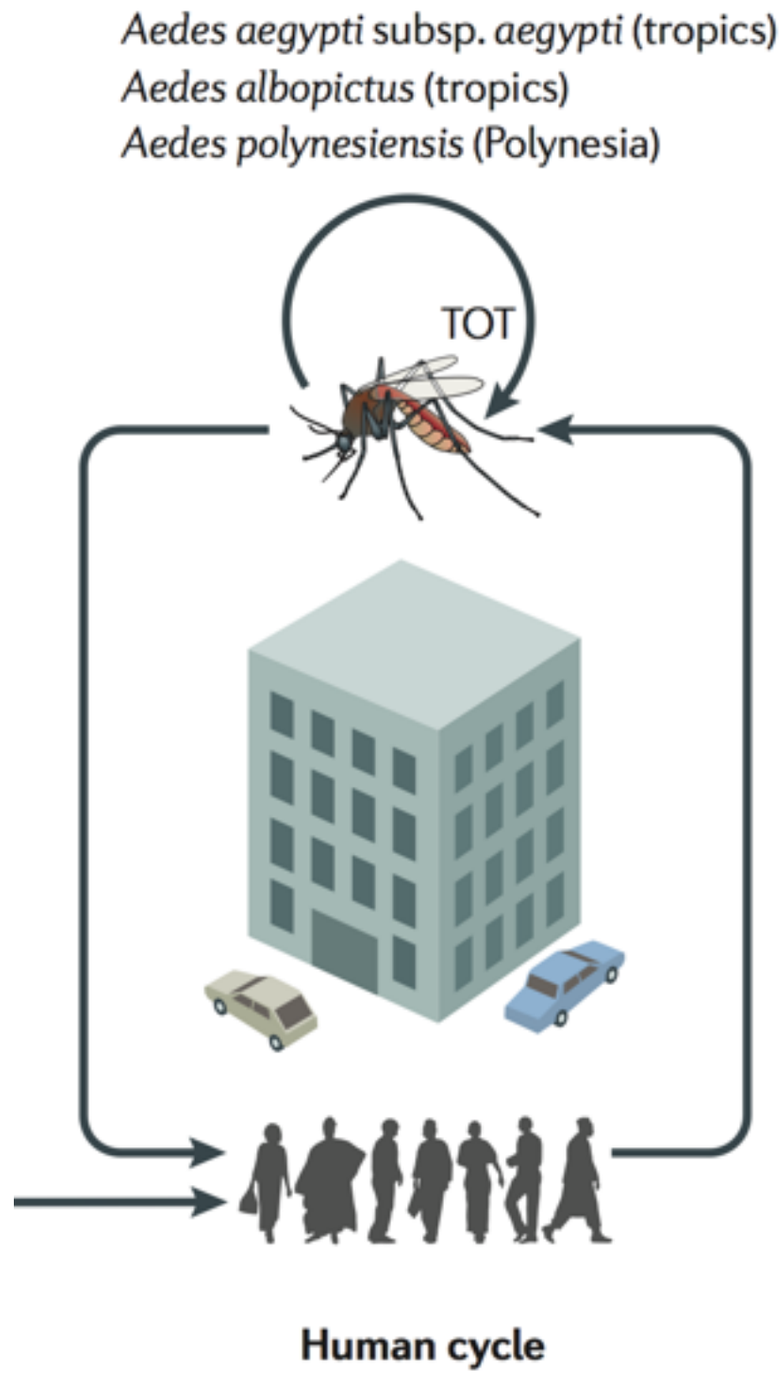
1. What is a sylvatic cycle?
2. Why would we think it is possible?
3. What is the probability of establishment?
4. What else do we need to know?

0. Zika Virus

- Isolated in 1947 in the Ziika forest of Uganda
- Flavivirus – ssRNA virus
- Transmitted by *Aedes* mosquitoes
- WHO PHEIC
- Mostly asymptomatic
- Rash, conjunctivitis, fever, arthralgia
- Emerging evidence for teratogenic effects and neurovirulence



Transmission cycles: human/endemic



Vasilakis et al., Nature Reviews Microbio, 2011

Transmission cycles: human/endemic

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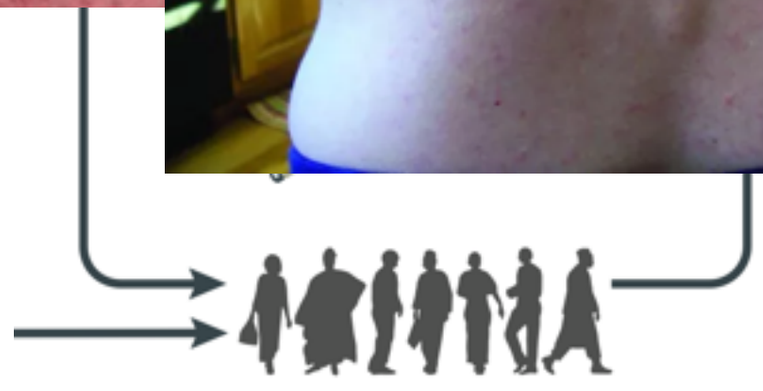

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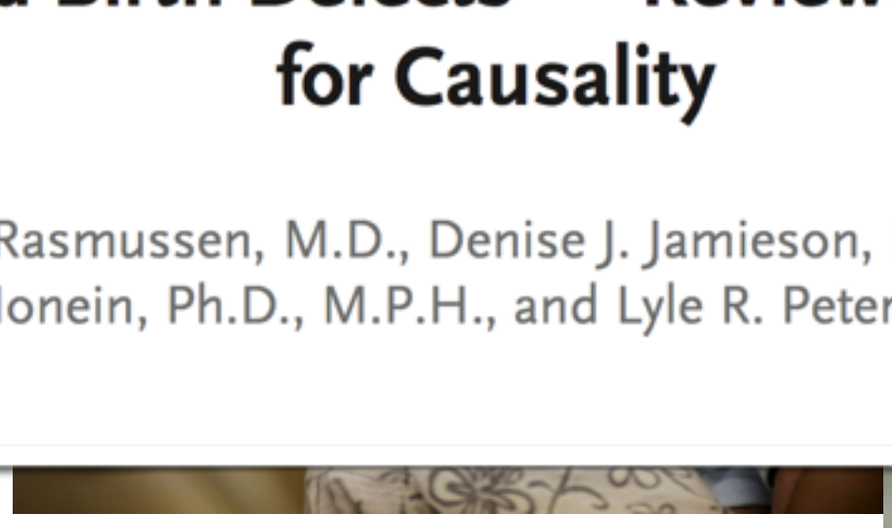
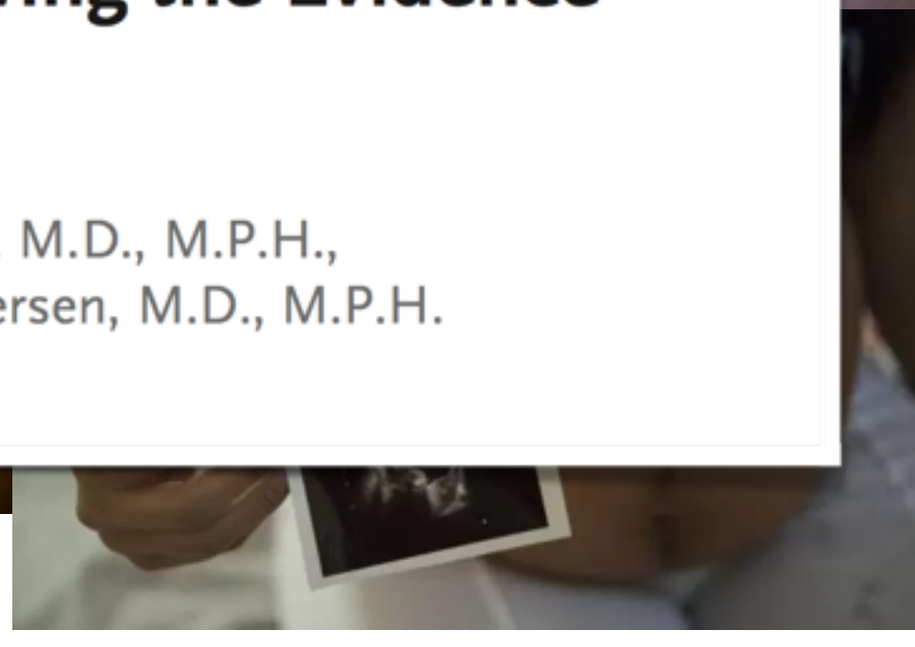
The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

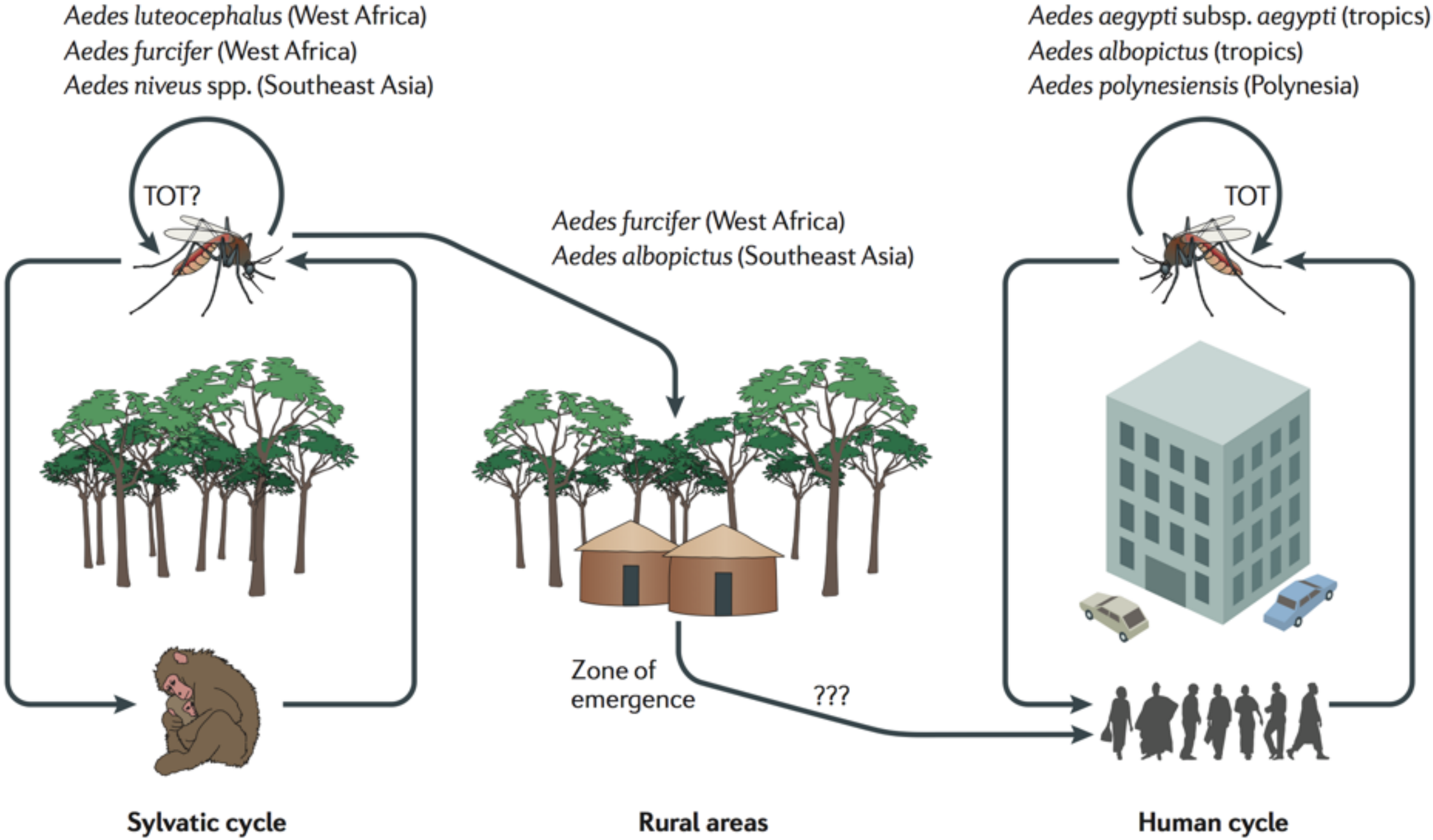
Zika Virus and Birth Defects — Reviewing the Evidence for Causality

Sonja A. Rasmussen, M.D., Denise J. Jamieson, M.D., M.P.H.,
Margaret A. Honein, Ph.D., M.P.H., and Lyle R. Petersen, M.D., M.P.H.





Transmission cycles: sylvatic/enzootic



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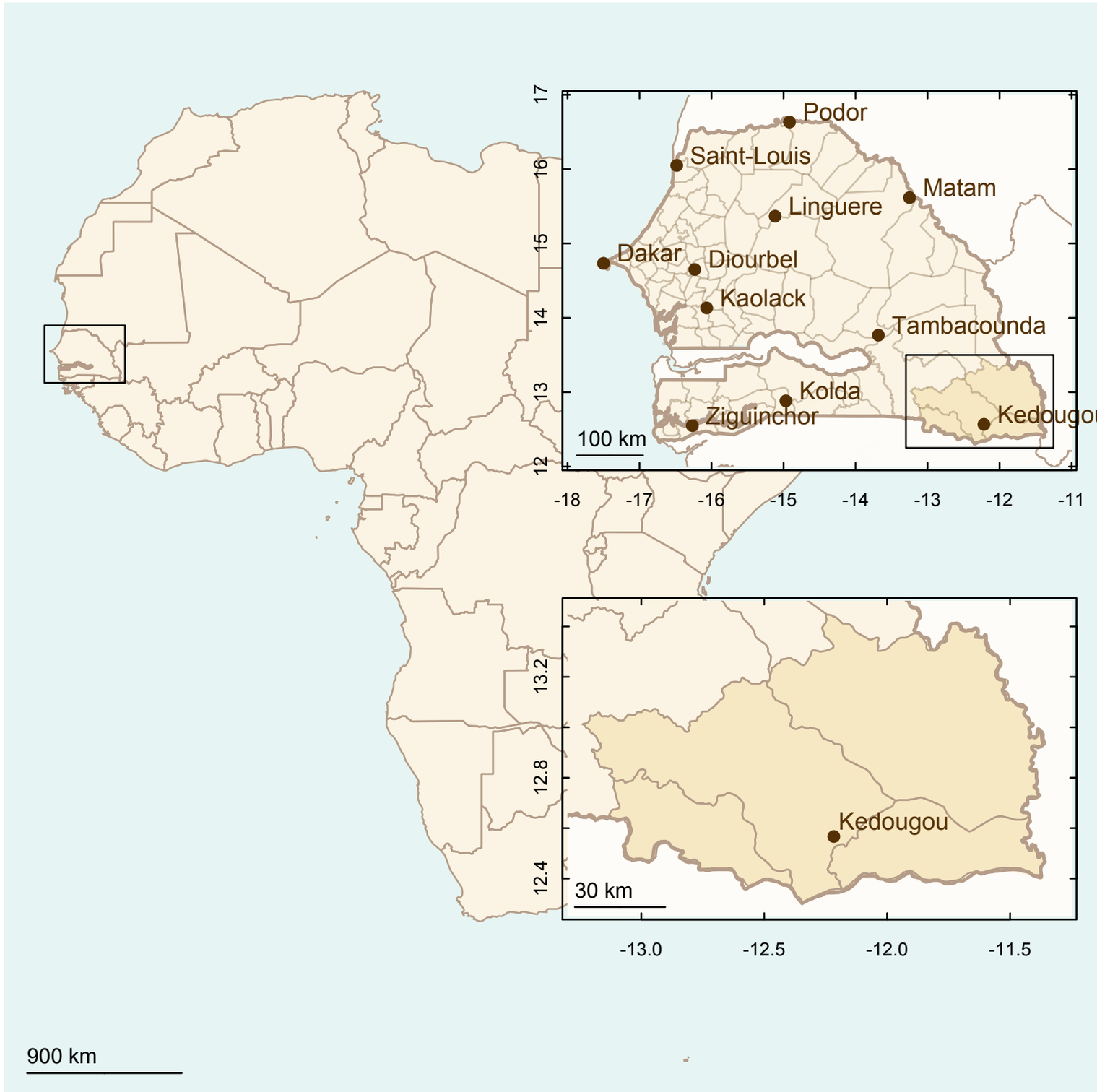
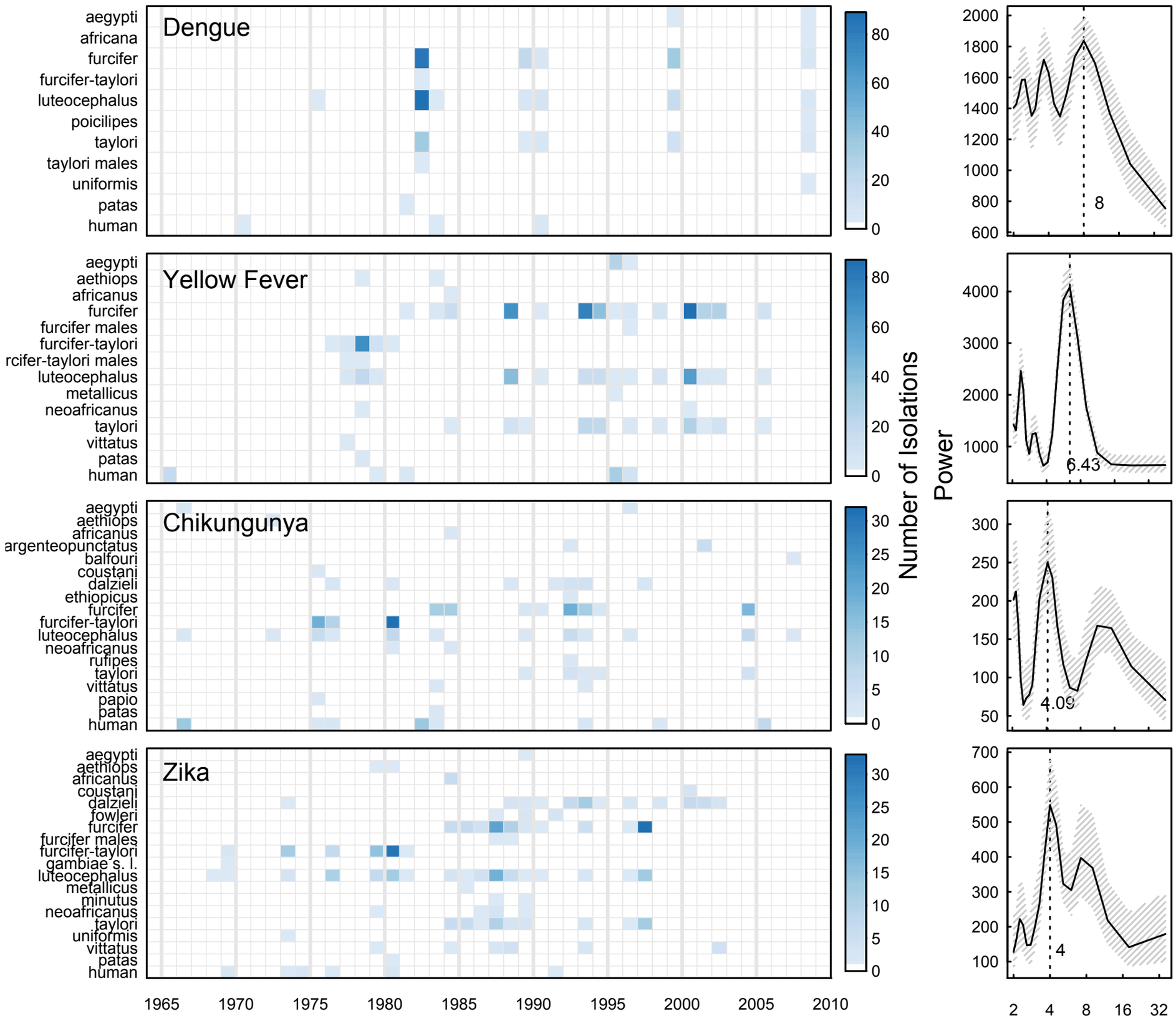
Sylvatic cycles in Africa

- Routine arbovirus surveillance by Institute Pasteur de Dakar
- 50 years of data
- Mosquito virus isolation
- Opportunistic primate isolation
- Expanded primate and mosquito sampling 2010-2012



Sylvatic cycles in Africa



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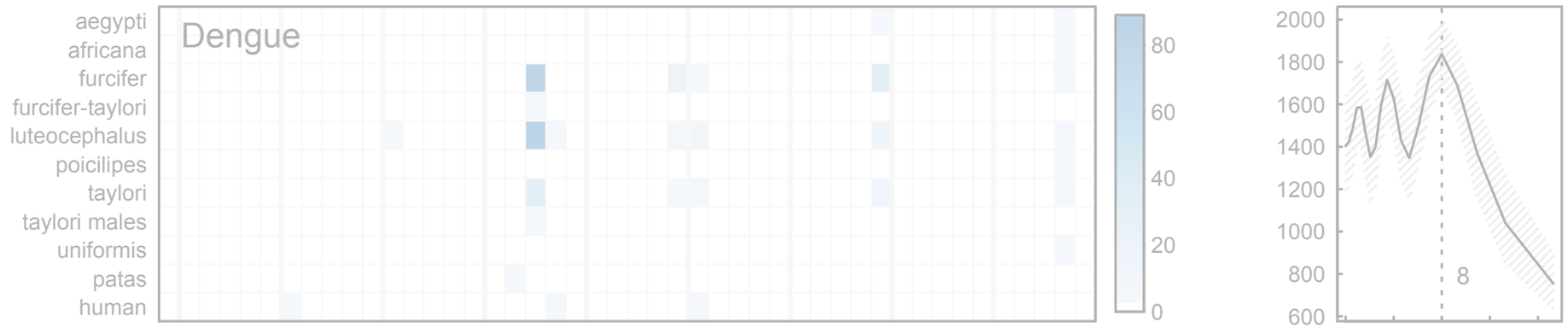
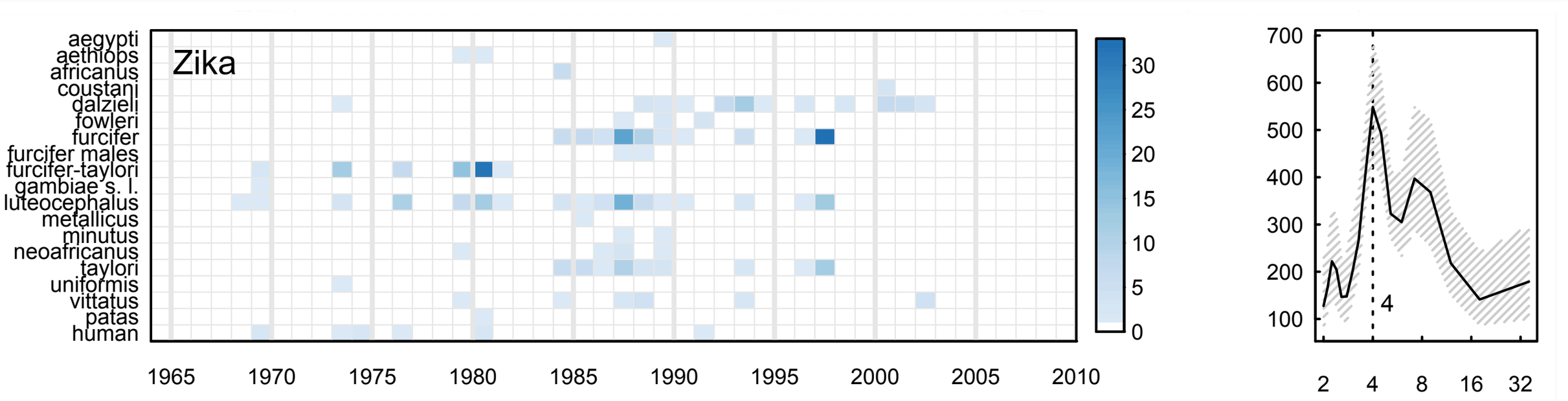
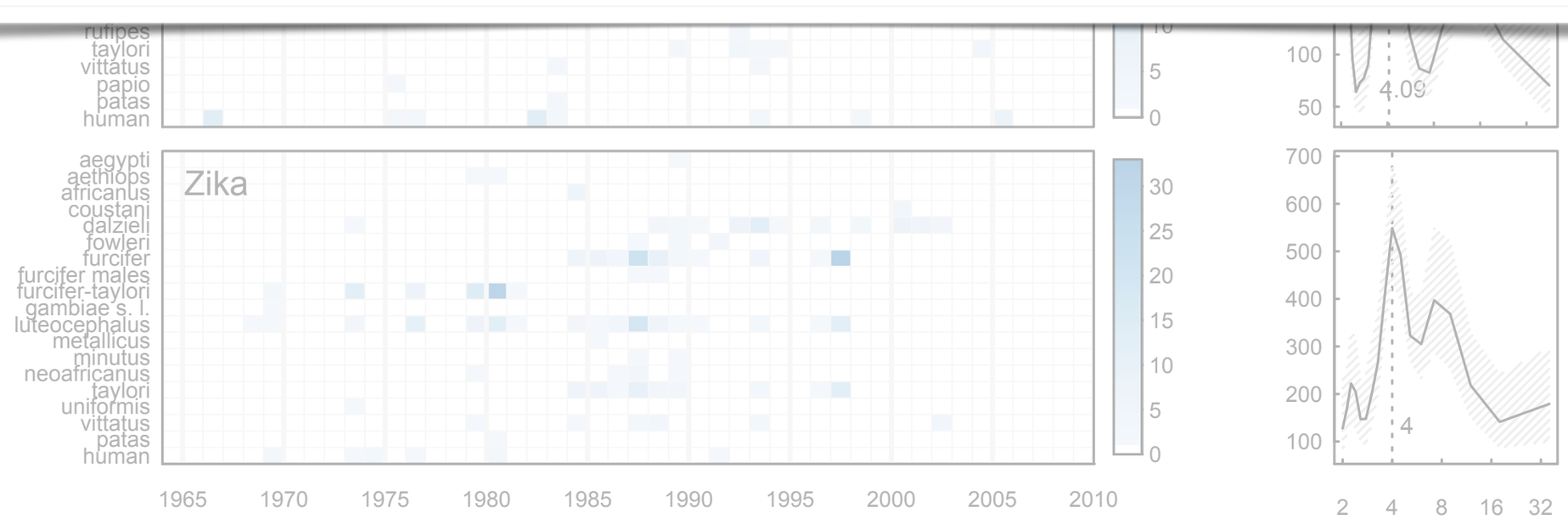






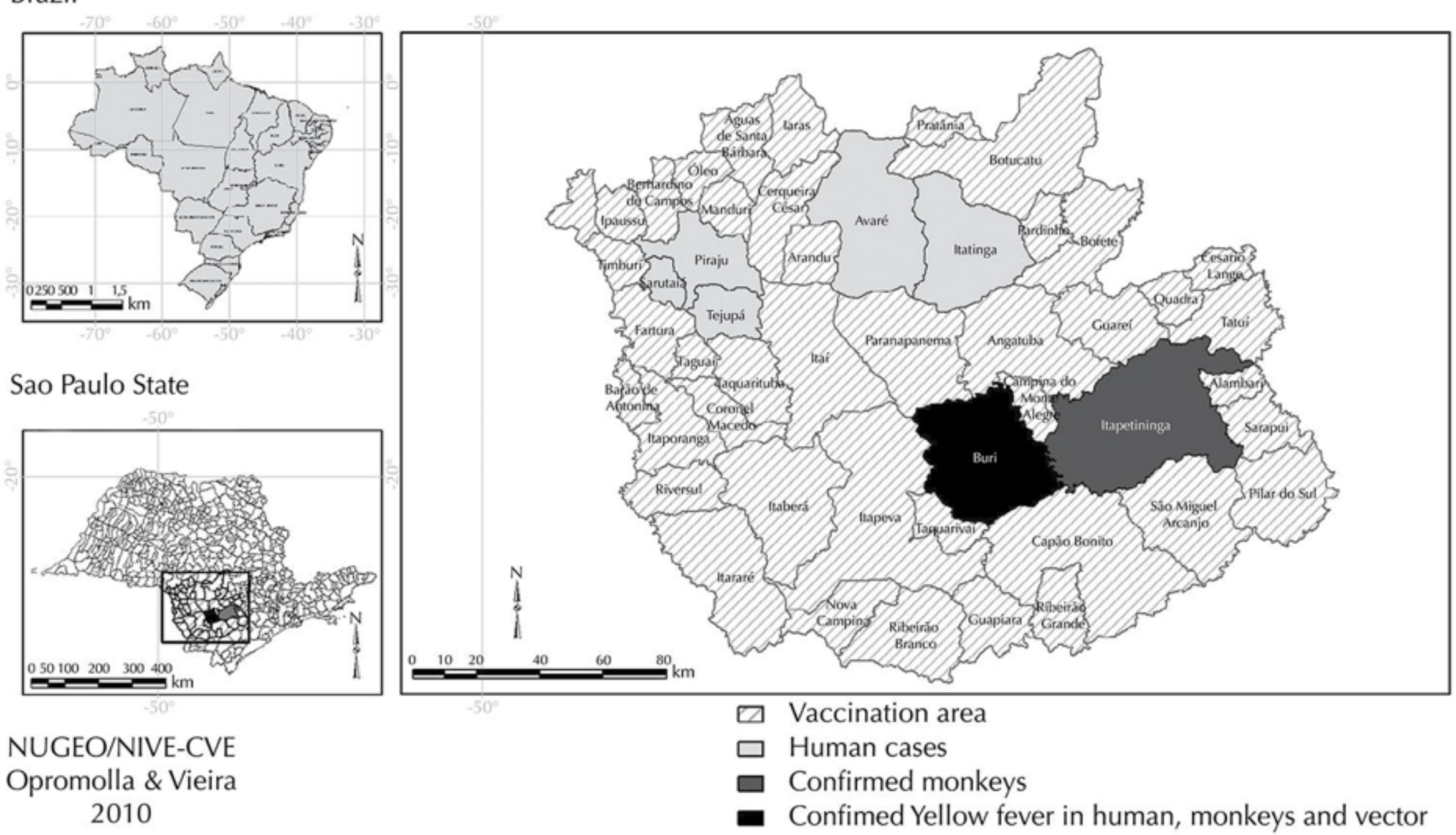
Sylvatic Zika in 2011

- 2011 saw an outbreak of Zika in Kedougou
- Zika isolated from 10 species of *Aedes*
  - *Ae. hirsutus, Ae. unilineatus, Ae. metallicus, and Ae. africanus* had highest infection rates
- Previous isolations in African green monkeys *(Chlorocebus sabaeus)* and patas monkeys *(Erythrocebus patas)*
- Isolated in rhesus macaque in Uganda
- ZEST team currently investigating Zika in rhesus macaque (https://zika.labkey.com/project/OConnor/ZIKV-001/begin.view)

Why do we think a sylvatic cycle is possible?

- Old World monkeys are susceptible to Zika virus infection
- Multiple mosquito species are susceptible to Zika virus infection
- *Both host and vector are present in South America*

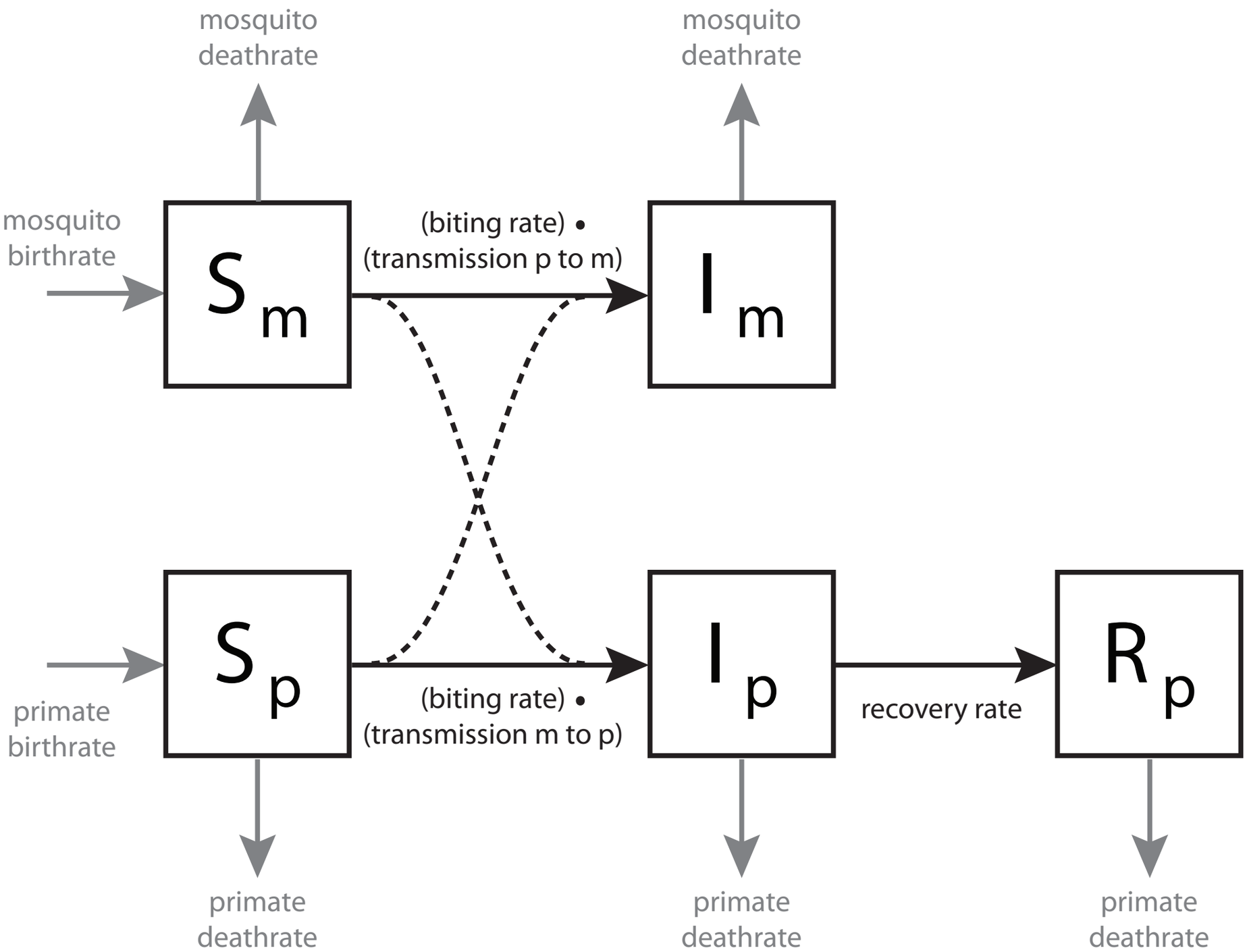
Yellow fever has an established sylvatic cycle

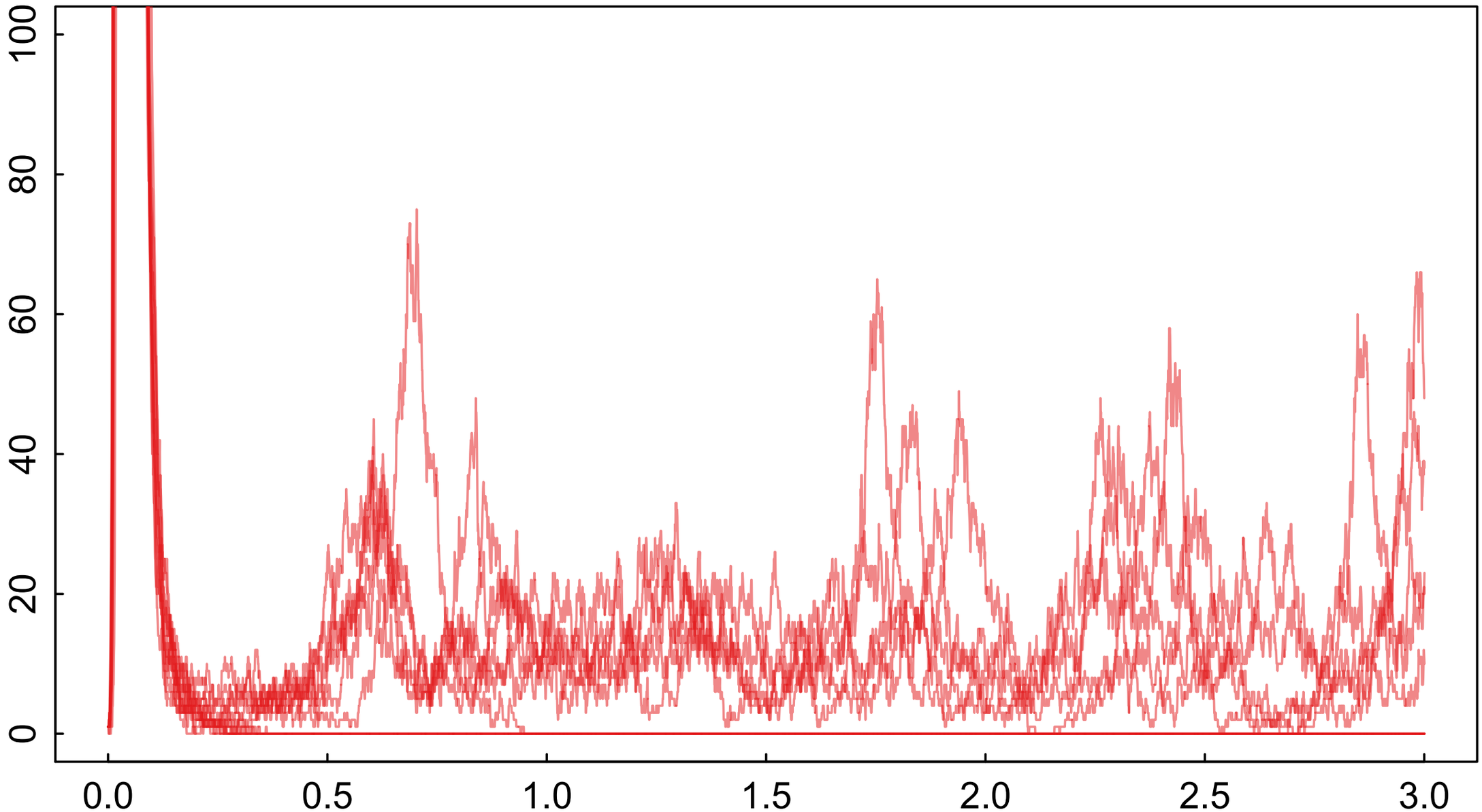


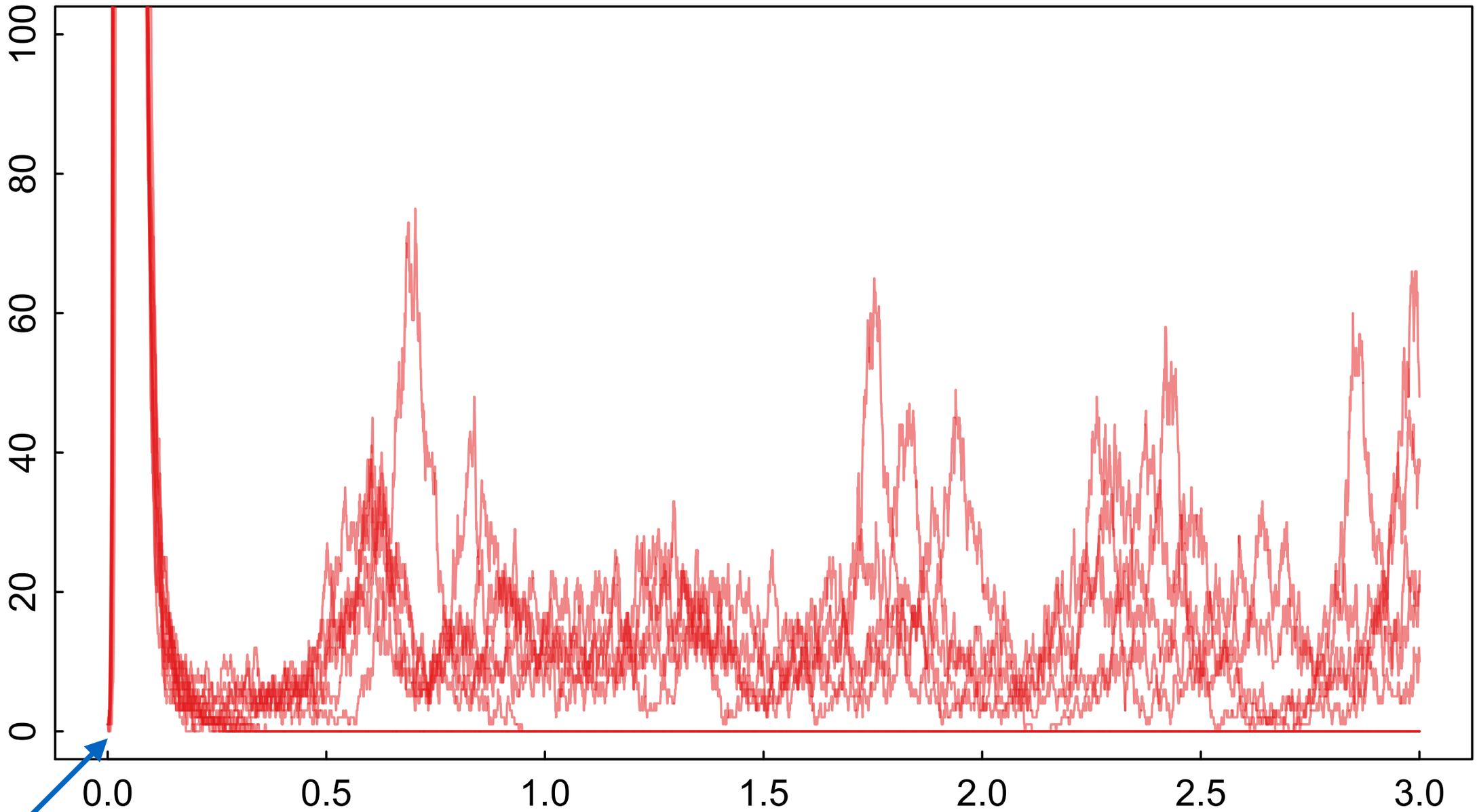
Source: *Sistema de Informação de Agravo de Notificação. Divisão de Zoonoses do Centro de Vigilância Epidemiológica. Coordenação de Controle de Doenças. Secretaria de Estado da Saúde de São Paulo.*

What is the probability of establishment?

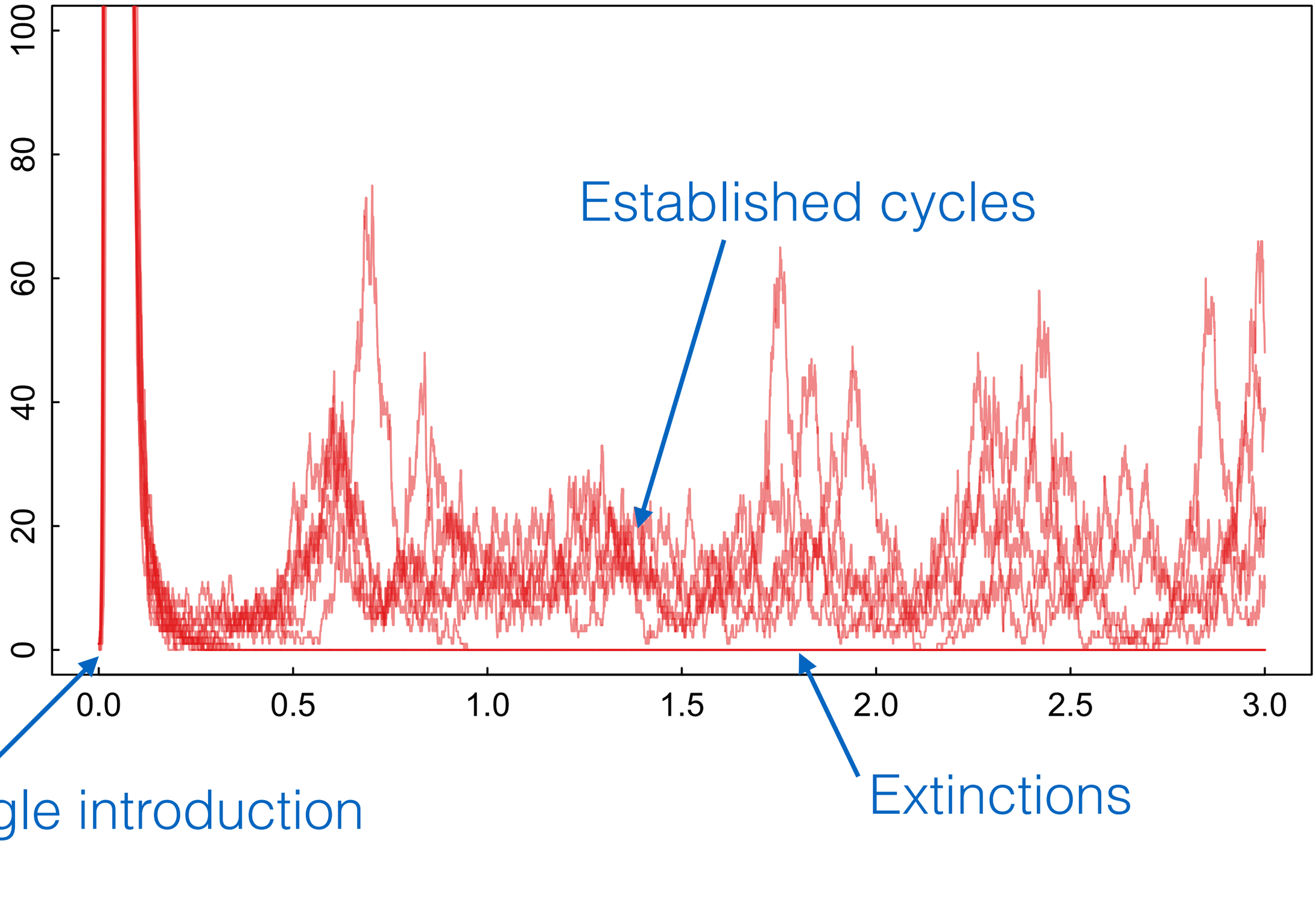
- Stochastic sylvatic transmission model (Gillespie)
- Parameterized using dengue virus transmission
- Single infectious introduction, no importation
- Multiple runs, find proportion that do not go extinct
- Key parameters:
  - Primate birthrate (lifespan)
  - Zika virus force of infection (infectious bites per day)


mosquito
deathrate
mosquito
deathrate
mosquito
birthrate
S m
(biting rate) •
(transmission p to m)
I m
S p
(biting rate) •
(transmission m to p)
I p
recovery rate
R p
primate
birthrate
primate
deathrate
primate
deathrate
primate
deathrate


0
20
40
60
80
100
0.0
0.5
1.0
1.5
2.0
2.5
3.0



Single introduction


100
80
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2.0
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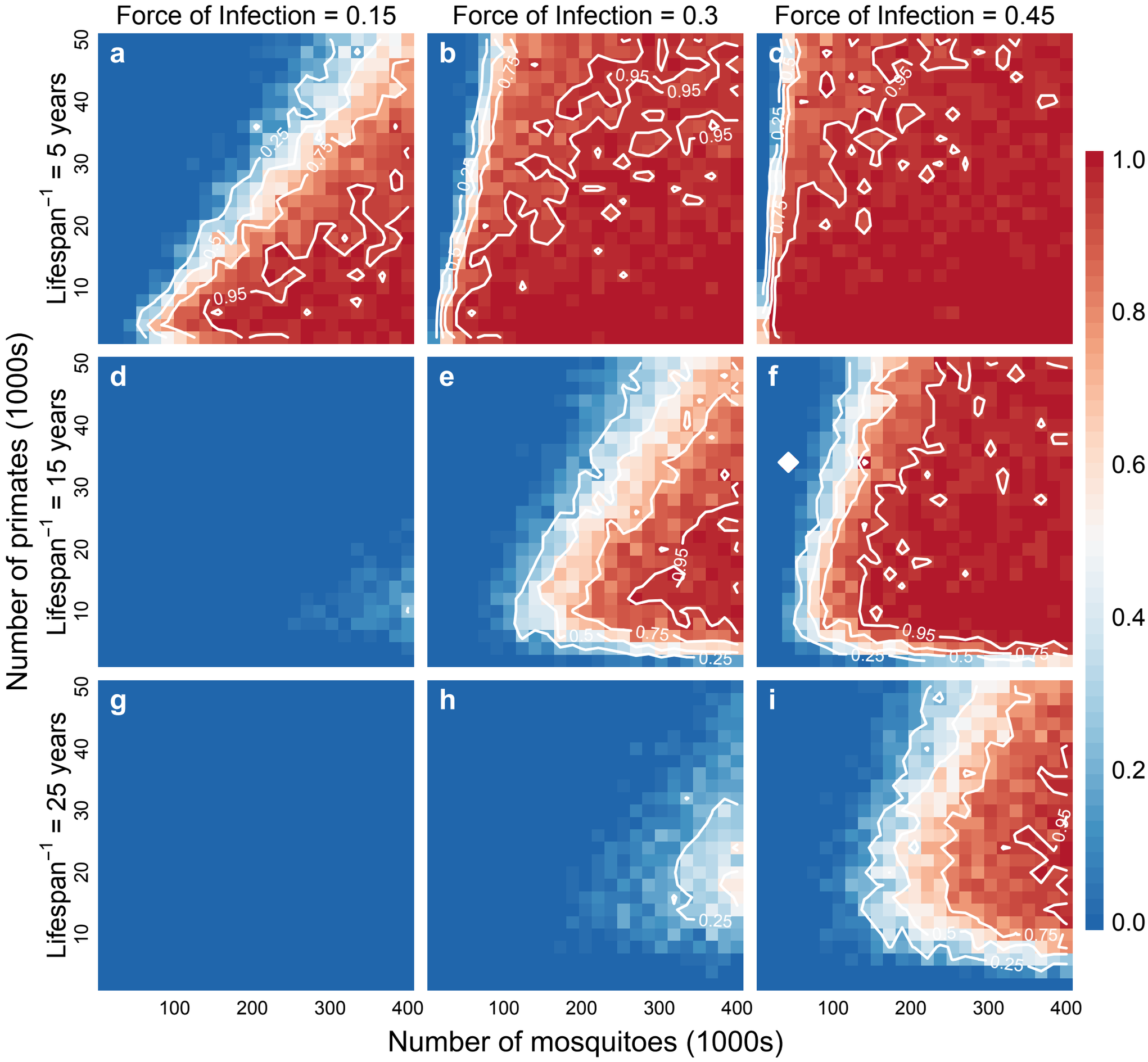
3.0
Established cycles
Single introduction
Extinctions


Force of Infection = 0.15
Force of Infection = 0.3
Force of Infection = 0.45
a
b
c
d
e
f
g
h
i
Lifespan^{-1} = 5 years
Lifespan^{-1} = 15 years
Lifespan^{-1} = 25 years
Number of primates (1000s)
Number of mosquitoes (1000s)
10
20
30
40
50
100
200
300
400
0.25
0.5
0.75
0.95
1.0
0.8
0.6
0.4
0.2
0.0

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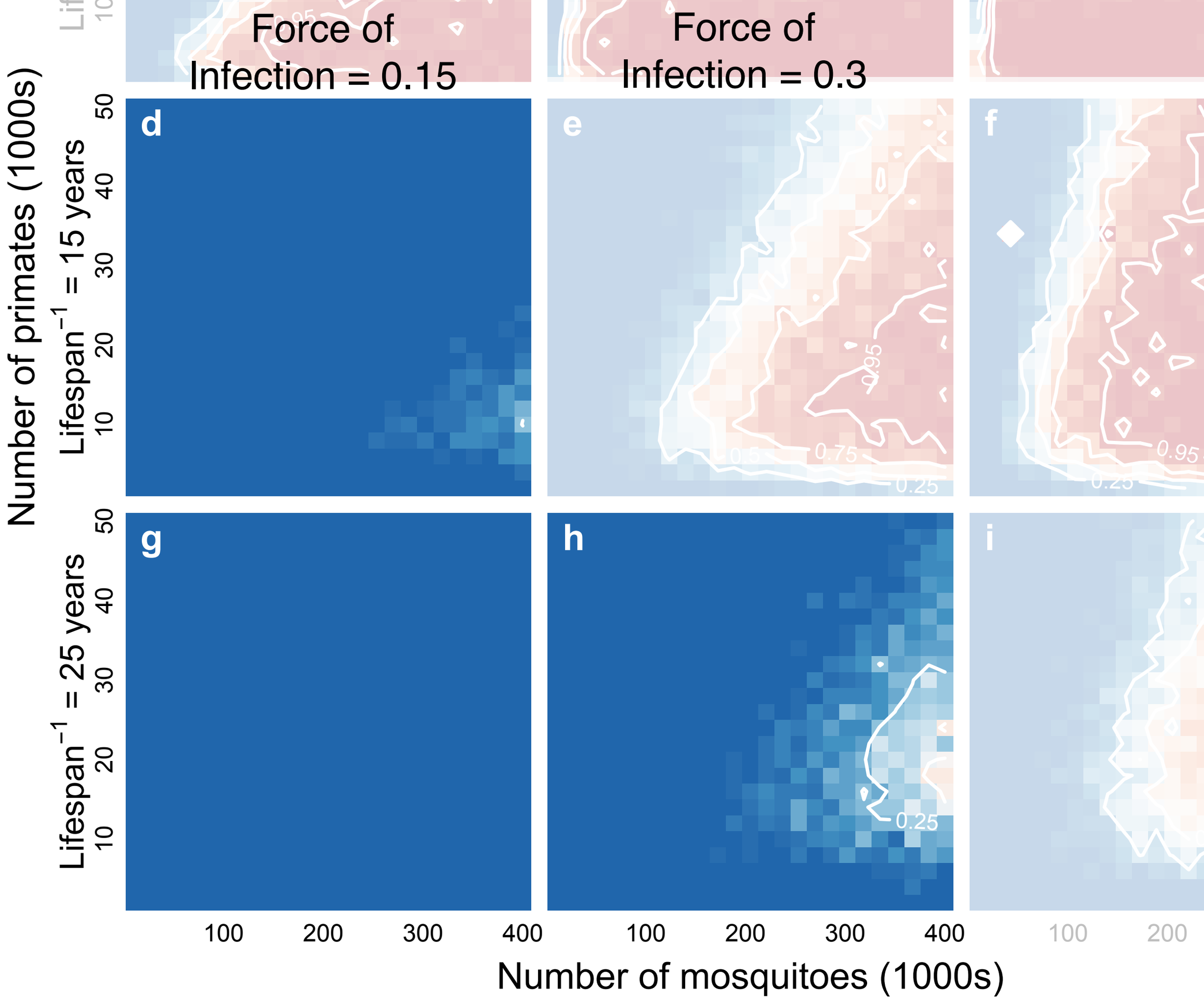

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a b c d e f g h i

0.25 0.5 0.75 0.95

10 20 30 40 50

100 200 300 400

1.0 0.8 0.6 0.4 0.2 0.0

What is the probability of establishment?

- High for a range of biologically realistic parameters
  - Higher birthrates -> higher probability (susceptible turn-over)
- Need more mosquitoes than primates
- But…

What else do we need to know?

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- Susceptibility of New World primates to Zika
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- Ranges of both these novel hosts and vectors
- The extent of a sylvatic dengue virus cycle (increased surveillance)

Outlook?

- Establishment of a sylvatic Zika virus cycle would make future elimination efforts impossible
- Requiring intensive surveillance and reactive mass vaccination in response to outbreaks

Thank you!

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http://biorxiv.org/content/early/2016/04/05/047175

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