IHME

Measuring what matters

Metapopulation models of infectious disease dynamics are sensitive to underlying host movement models

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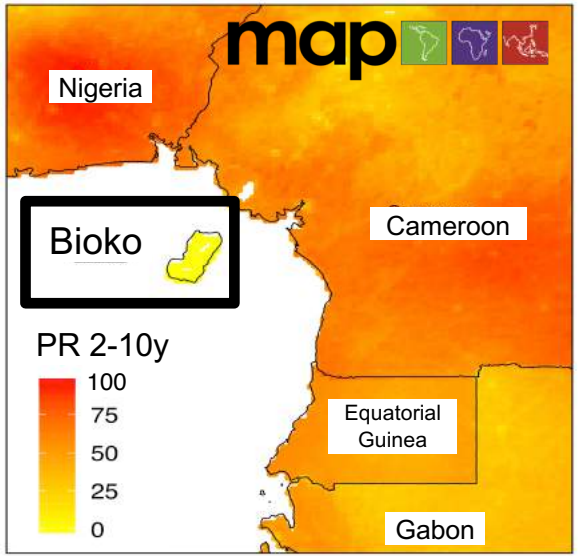
Simulating Malaria Transmission

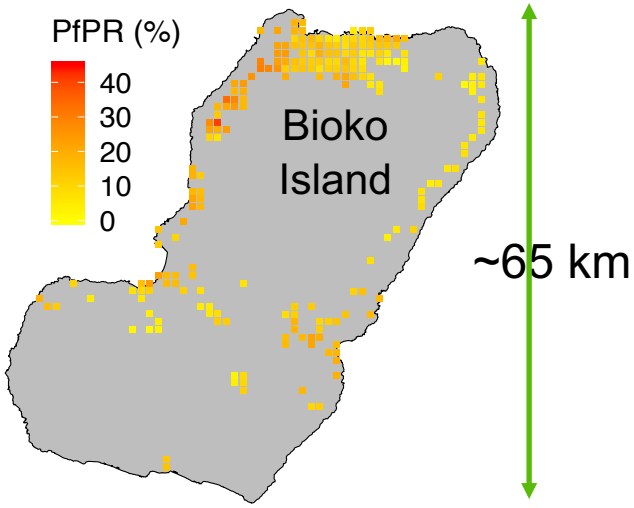
- Our group builds mechanistic simulation models of malaria transmission
- Malaria
  - Parasitic disease
  - Vector-borne – *Anopheles* mosquitoes
  - Tropical climates

- An ecological disease
  - Risk of infection *strongly* dictated by local environment
  - Transmission intensities can vary dramatically, even across short distances
- Simulation models representing the real world require knowing how transmission intensities vary in geographical space

Malaria Prevalence Mapping

- Geostatistical estimates of Parasite Rate (PR) – a measure of prevalence
- Example: Bioko Island, Equatorial Guinea
  - Low transmission location, surrounded by high-transmission locations
  - Island residents who travel are highly likely to bring back infections with them





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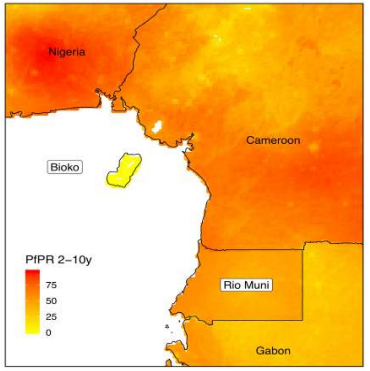
Transmission Intensity Estimation

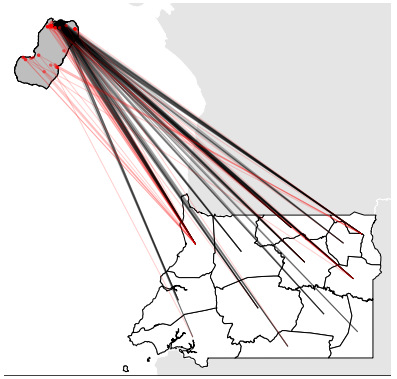
- Start with data inputs:
  - Prevalence maps
  - Travel survey data
- Combine with simulation model
  - Transmission model – how infection spreads
  - Movement model – how people move
- Goal: Estimate transmission intensity
  - Map of PR ⟶ Map of R_0
  - How high does R_0 need to be to produce the PR levels seen in the maps?

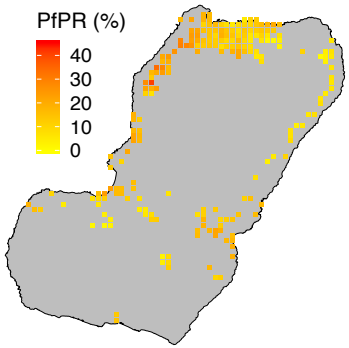
Data Inputs

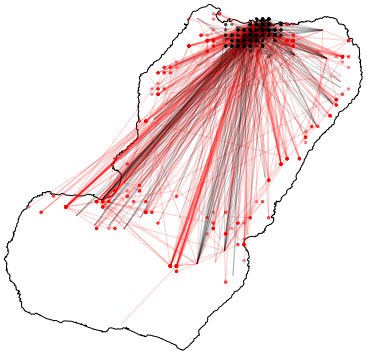
Prevalence



Travel

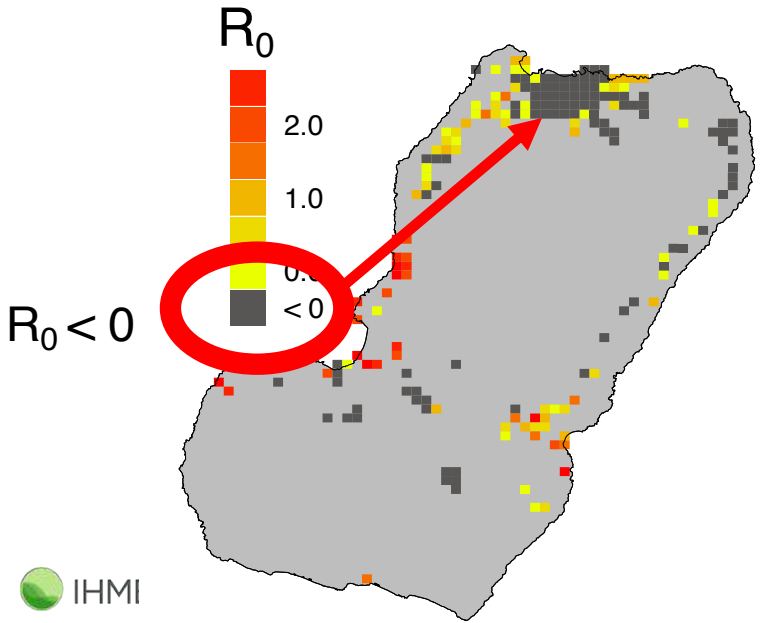


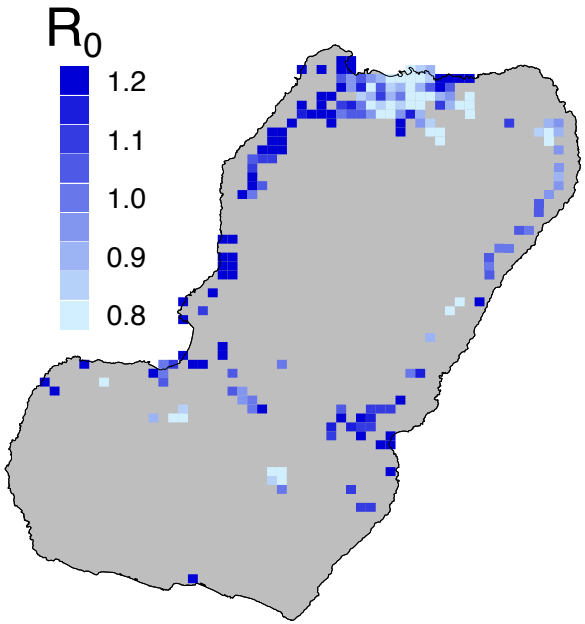




Sensitivity to Movement Model

- R_0 estimation, using 2 different candidate movement models
  - Same input data
  - Same transmission model





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Metapopulation Movement Models

- Metapopulation
  - epidemiologically isolated population which interacts weakly with other populations
  - e.g. geographically isolated; interact through infrequent human travel

- Movement models: the rules which govern how people travel
  - Who travels?
  - How frequently do they travel?
  - Where do they go?
  - How long do they spend away?

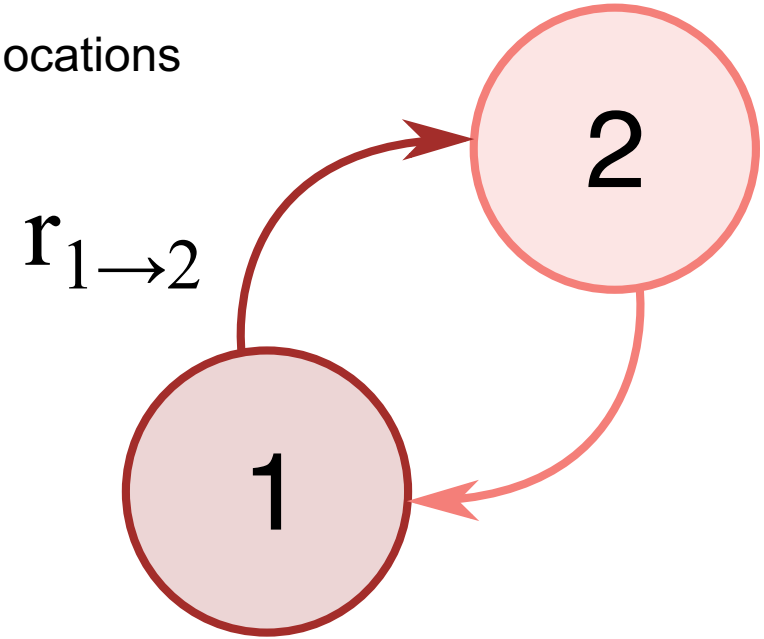
Movement Models – Flux model

- "Flux model" -or- "Eulerian model"
- Planktonic – hosts diffuse between metapopulations
- "How many people moved from here to there?"
- One rate for each origin-destination pair of locations
  - The rate at which residents leave

$$\frac{dN_1}{dt} = r_{2\to1}N_2 - r_{1\to2}N_1$$

$$\frac{dN_2}{dt} = r_{1\to2}N_1 - r_{2\to1}N_2$$

$$N = N_1 + N_2$$



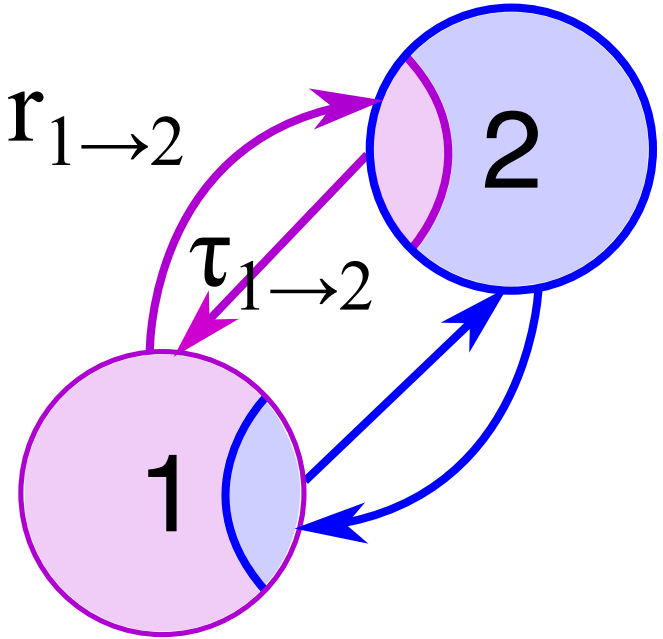
Movement Models – Time at Risk

- "Time at risk model" -or- "Lagrangian model"
- "How many people moved from here to there?" & "How long did they stay there?"
- Two rates per origin-destination pair
  - The rate at which residents leave
  - The rate at which travelers return

$$\frac{dN_{1,1}}{dt} = \tau_{1\to2}N_{1,2} - r_{1\to2}N_{1,1}$$

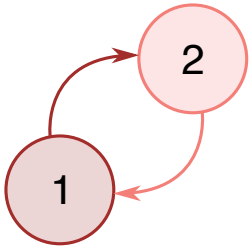
$$\frac{dN_{1,2}}{dt} = r_{1\to2}N_{1,1} - \tau_{1\to2}N_{1,2}$$

$$N_1 = N_{1,1} + N_{1,2}$$



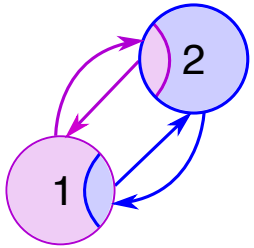
Movement Model Comparison

Flux:



- Data sources:
  - Census migration data
  - Cell phone call location records
- Fewer parameters

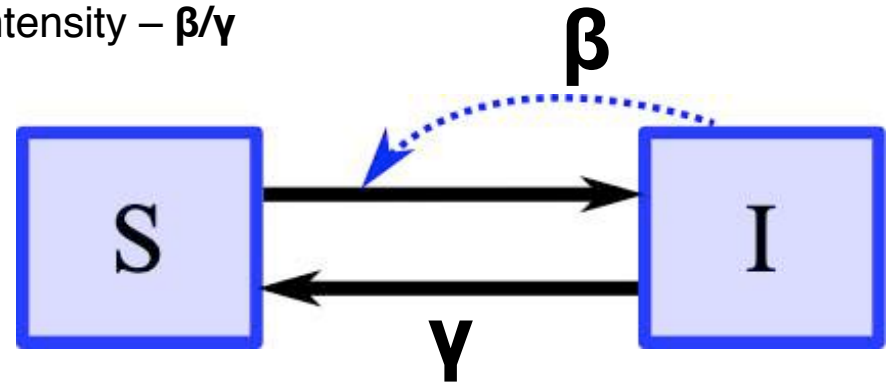
Time at Risk:



- Requires knowing travel duration
- Data sources:
  - GPS trip loggers
  - Travel survey
- Specify time spent away while traveling

Disease Transmission Modeling

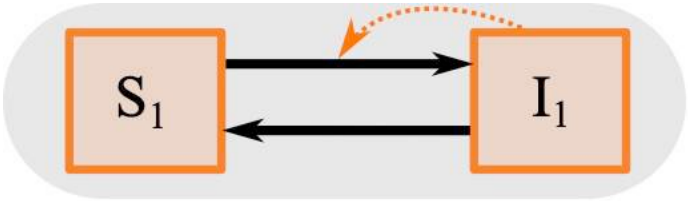
- Example: Susceptible-Infected-Susceptible Model
  - Will be showing numerical results from ODEs
  - Malaria-related models are more complicated, but still comparable to SIS
- Parameters that matter:
  - Duration of Infection: 1/**γ**
  - Transmission intensity – **β/γ**



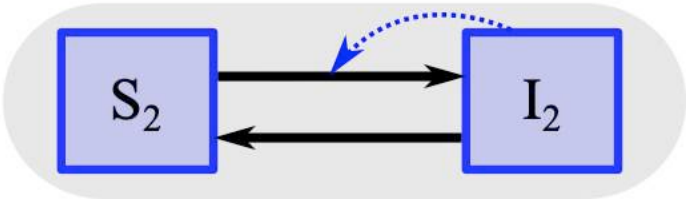
Metapopulation Transmission Models

- What rules do we use to allow these metapopulations to interact?

Metapopulation 1

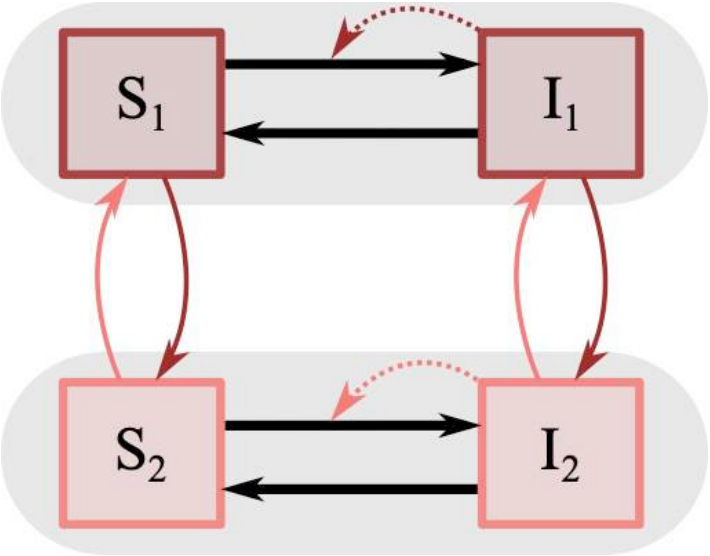


Metapopulation 2

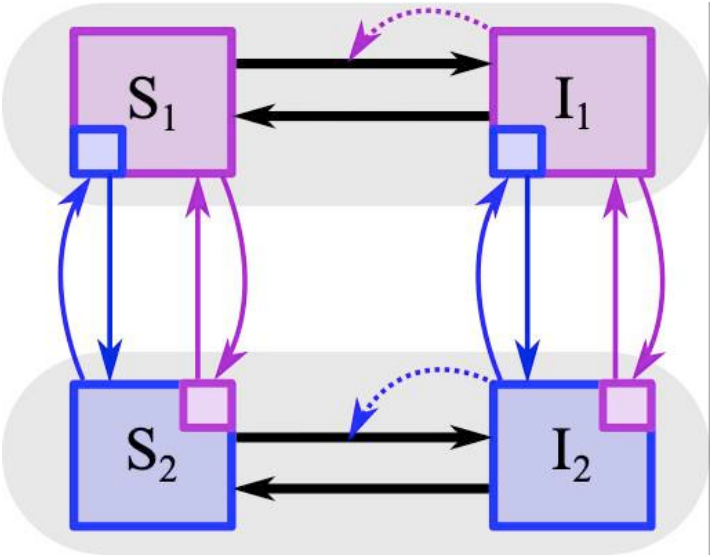


Transmission + Movement

Flux:



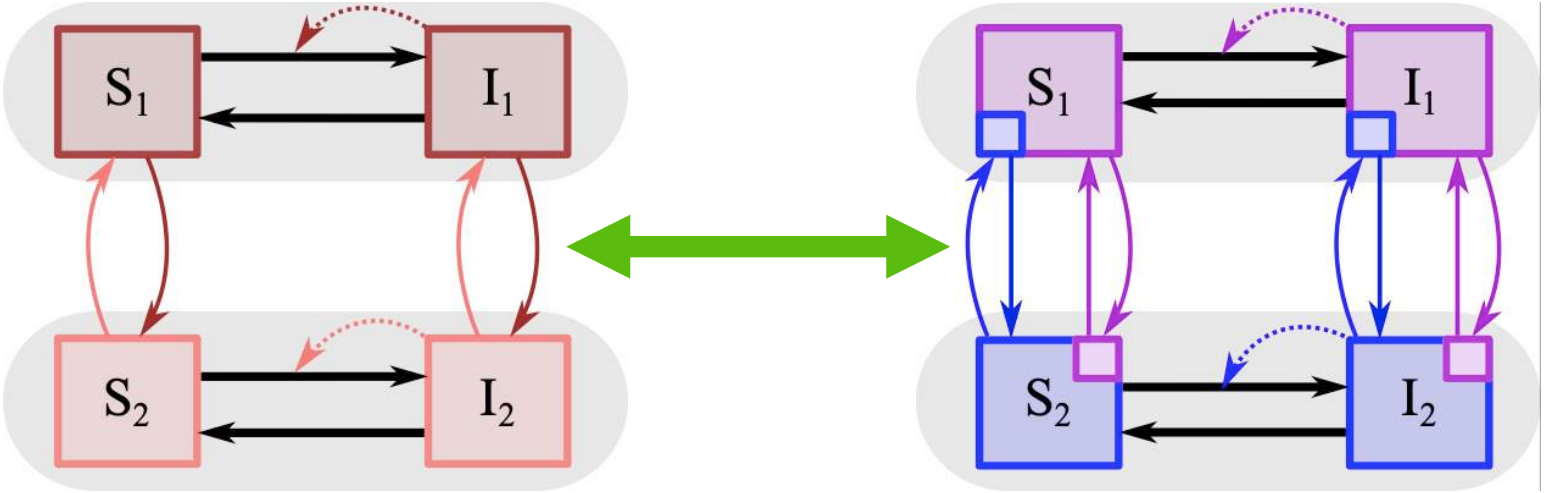
Time at Risk:



- Combine our metapopulation disease model with our two movement models

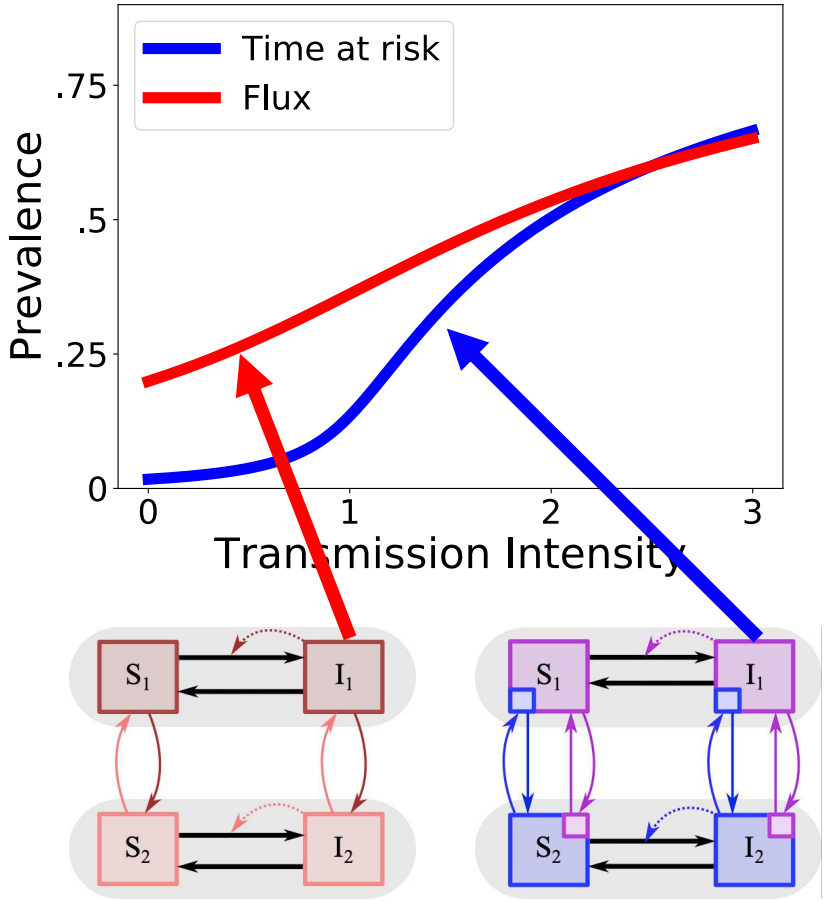
Direct Model Comparison

- Imagine calibrating to same movement data
- Set movement parameters to match total number of people moving from 1→2 or from 2→1 for both models



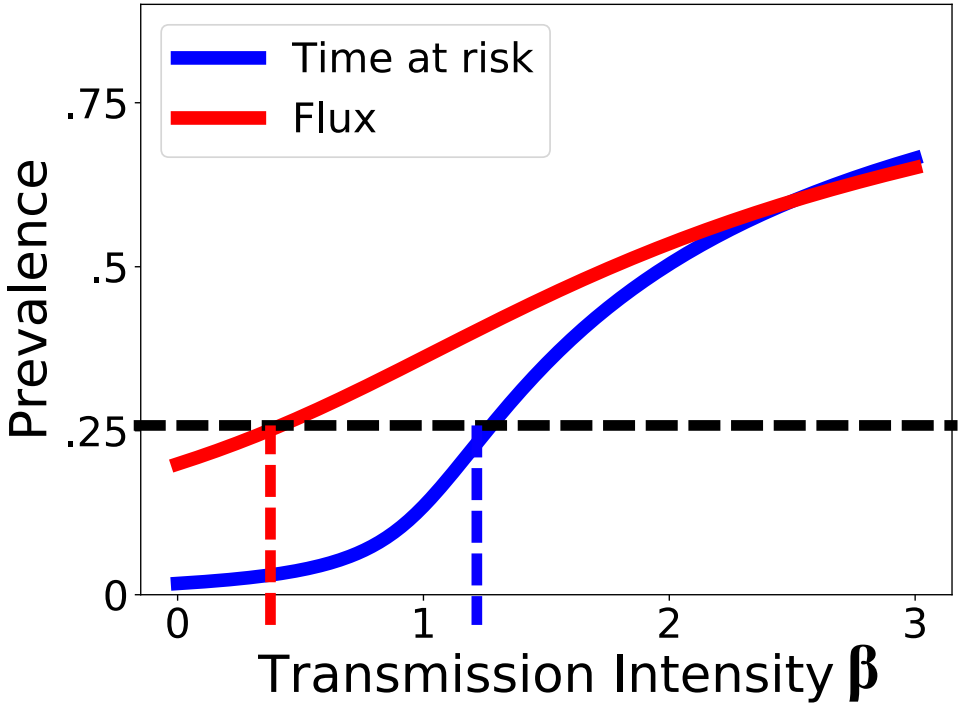
Movement Model Comparison

- Parameters that matter:
  - Infectious period: $1/\gamma$
  - Transmission intensity - β/γ
  - Duration of travel - r/γ
- Imagine one scenario:
  - ($\gamma=1$)
  - "Short Travel" $r/\gamma > 1$
  - High transmission in location 2: $\beta/\gamma > 1$
  - Measure location 1 Prevalence (I_1) as we vary β in location 1



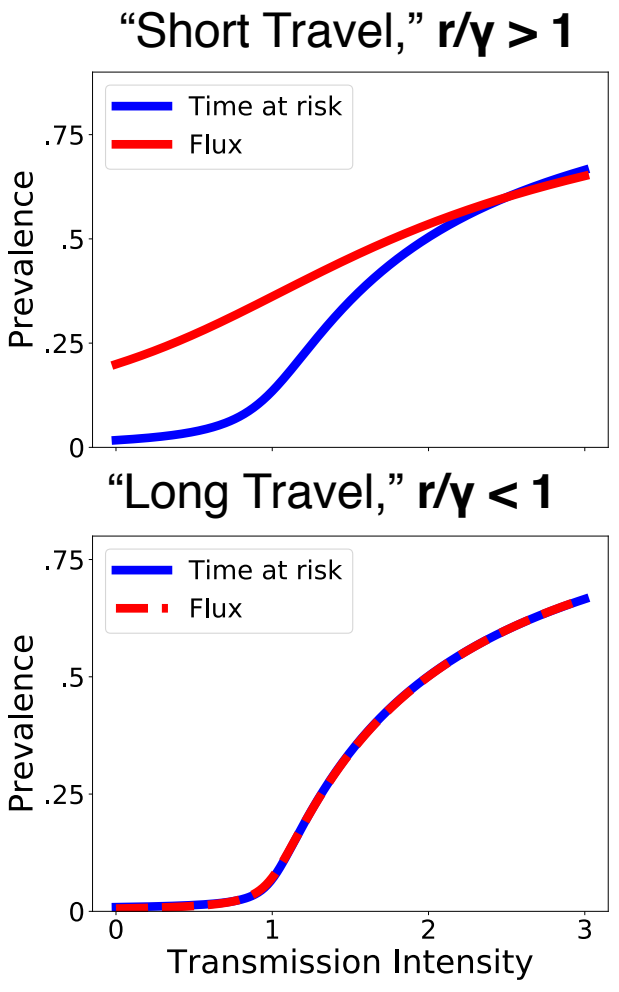
Mismatched predictions

- Infer intensity from prevalence
  - Flux model predicts **β < 1**
  - Time at Risk model predicts **β > 1**
- We can start from the same data and same transmission models, we get very different results!



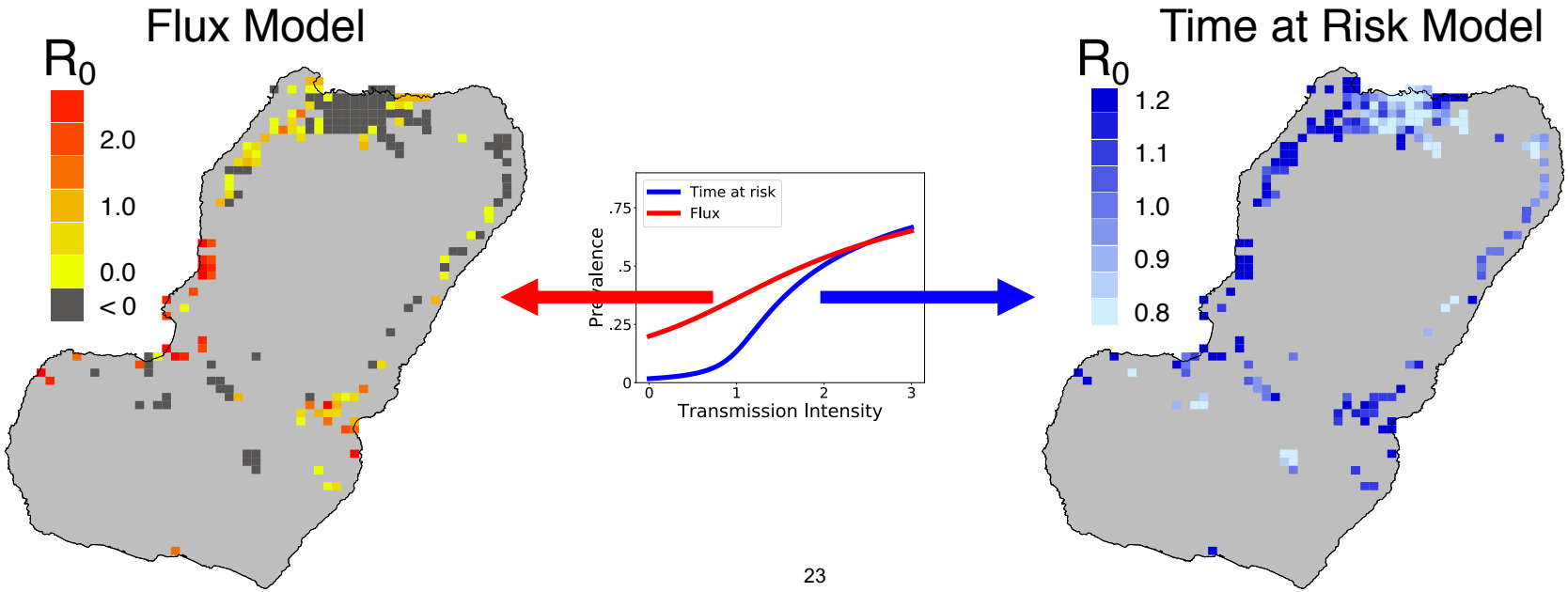
Other parameter regimes

- Disagreement when travel duration is shorter than infectious period
  - (Malaria $1/\gamma \approx 200$ days)
- Agreement when travel duration is bigger than infectious period
- Suggests a mechanism for the disagreement:
  - When travel is short, the Time at Risk model constrains the amount of time people spend at risk while traveling; the Flux model does not



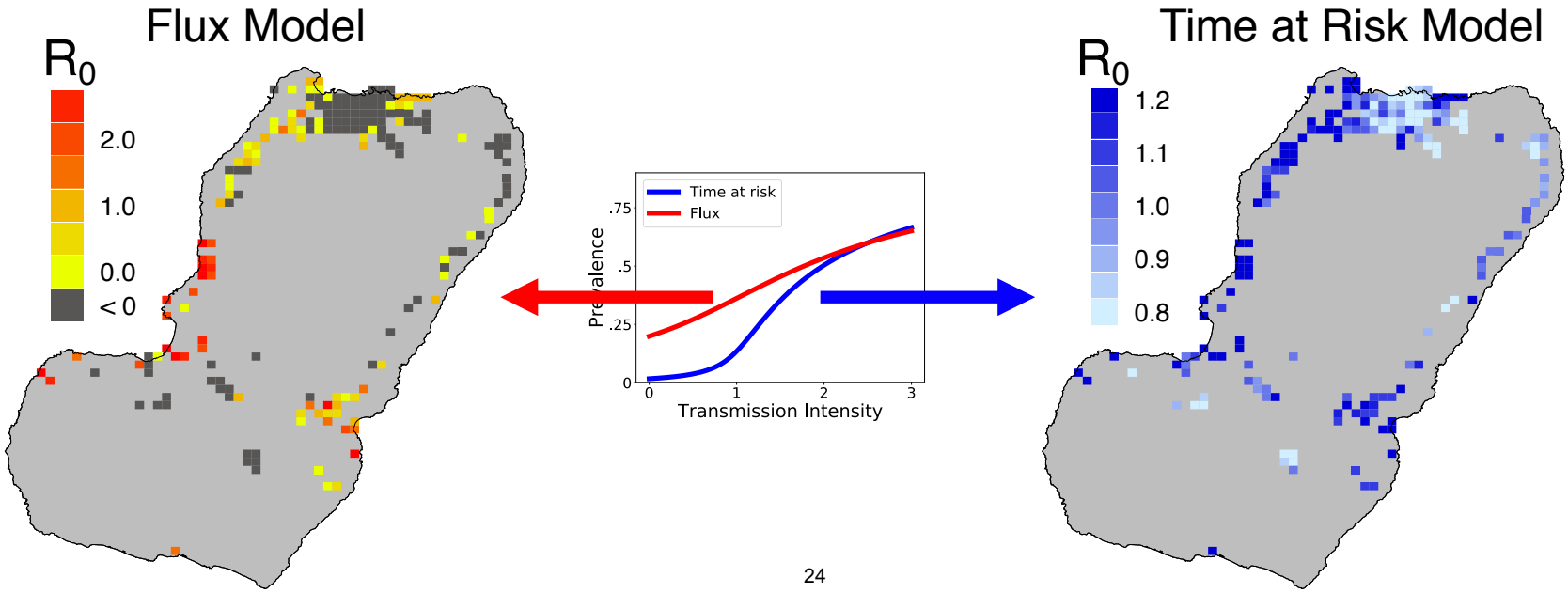
Return to Malaria

- Bioko Island: a low transmission region where people frequently travel to a high transmission region
- Estimate R_0 using same prevalence and travel data



Return to Malaria

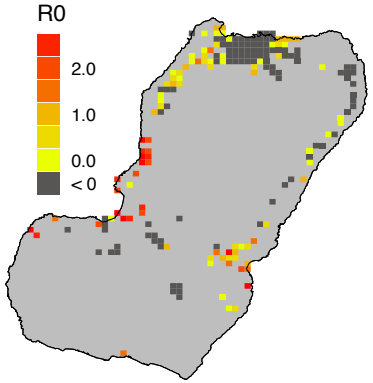
- Time at Risk model allows us to correctly specify the amount of time spent at risk while traveling, especially off-island
- The Flux model overestimates risk; produces nonsensical results



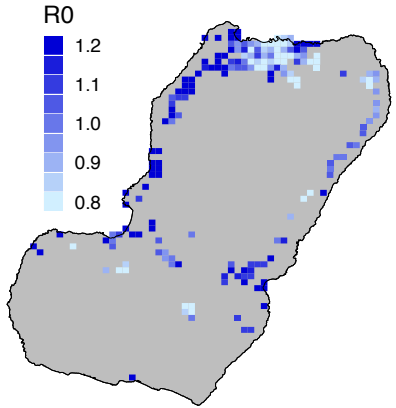
Lessons Learned

- Using simulations that combine models of disease transmission and host movement
- The choice of movement model really matters
- The difference is most important when travel occurs over a short period of time compared to the disease infectious period
- Being careful when using Flux models
  - Easier to parameterize (half as many parameters)
  - Recent availability of call data records and other data sets
  - But this doesn't mean we can always use the Flux model and obtain accurate epidemiological answers

Flux Model



Time at Risk Model



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- Katherine Battle, Harry Gibson, Dan Weiss (MAP collaborators)
- Joel Miller, Drew Dolgert, Robert Reiner, John Henry, Hector Sanchez

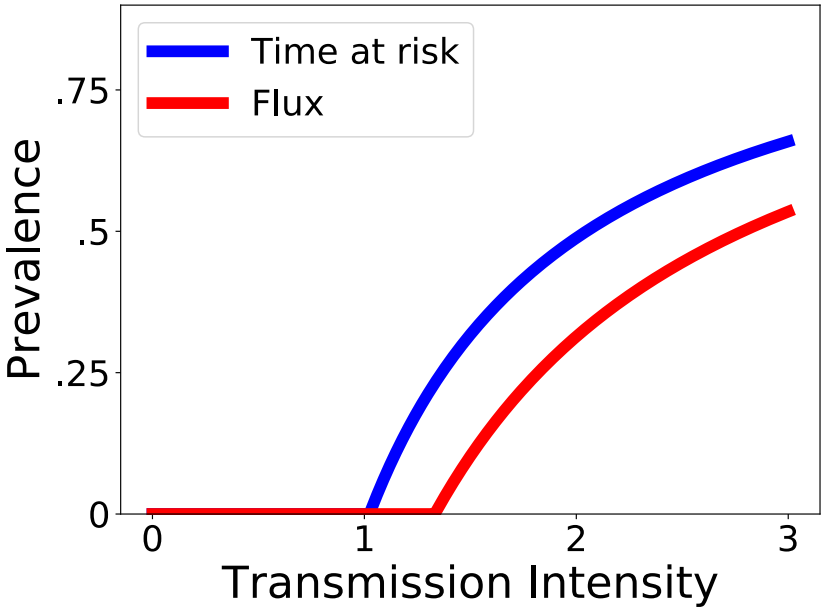
Sources

1. Cosner, C., et al. (2009). The effects of human movement on the persistence of vector-borne diseases. *J. of Theo. Bio.*, *258*(4), 550–560
2. Ruktanonchai, N. W., et al. (2016). Identifying Malaria Transmission Foci for Elimination Using Human Mobility Data. *PLoS Computational Biology*, *12*(4).
3. Bradley, John, et al. "Infection importation: a key challenge to malaria elimination on Bioko Island, Equatorial Guinea." *Malaria journal* 14, no. 1 (2015): 46.
4. Guerra, Carlos A., et al. "Human mobility patterns and malaria importation on Bioko Island." *Nature comms.* 10, no. 1 (2019): 2332.

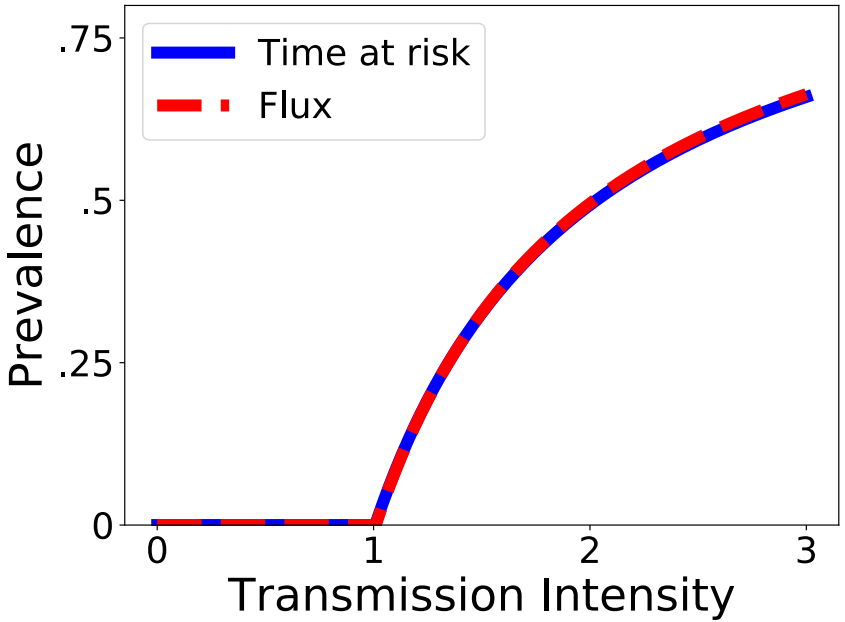
Other parameter regimes

- Traveling from endemic setting to low-transmission setting

"Short Travel," **r/γ > 1**



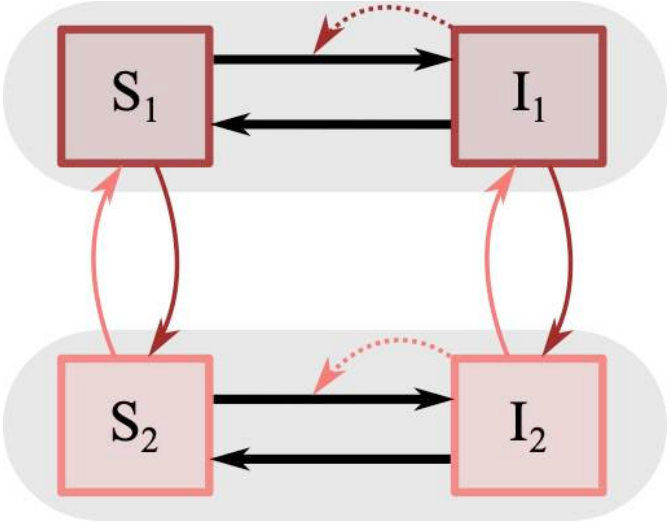
"Long Travel," **r/γ < 1**



SIS + Flux Model Equations

For two metapopulations:

$$\frac{dI_1}{dt} = \underbrace{\beta_1 I_1(N_1 - I_1) - \gamma I_1}_{\text{Transmission}} - \underbrace{r_{1,2} I_1}_{\text{Leaving}} + \underbrace{r_{2,1} I_2}_{\text{Arriving}}$$



For any number of metapopulations:

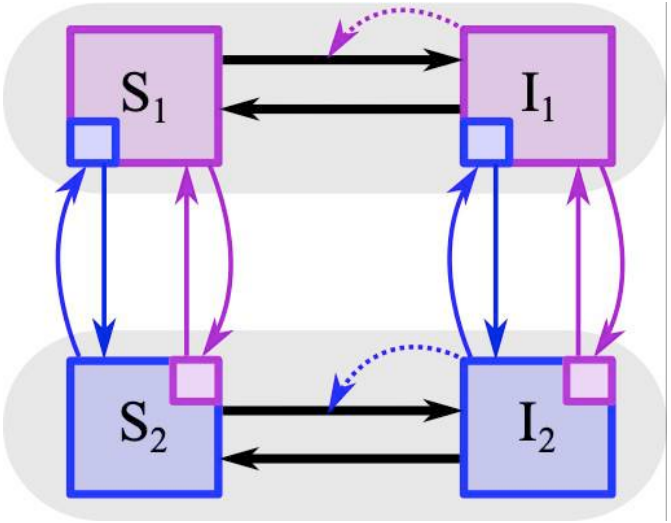
$$\frac{dI_i}{dt} = \underbrace{\beta_i I_i(N_i - I_i) - \gamma I_i}_{\text{Transmission}} - \underbrace{\sum_{j \neq i} r_{i,j} I_i}_{\text{Leaving}} + \underbrace{\sum_{j \neq i} r_{j,i} I_j}_{\text{Arriving}}$$

SIS + Time at Risk Equations

For any number of metapopulations:

$$\frac{dI_{i,i}}{dt} = \underbrace{\frac{\beta_i \sum_k I_{k,i}}{\sum_k N_{k,i}} (N_{i,i} - I_{i,i}) - \gamma I_{i,i}}_{\text{Transmission}} - \underbrace{\sum_{k \neq i} r_{i,k} I_{i,i}}_{\text{Outbound}} + \underbrace{\sum_k \tau_{i,k} I_{i,k}}_{\text{Inbound}}$$

$$\frac{dI_{i,j}}{dt} = \underbrace{\frac{\beta_j \sum_k I_{k,j}}{\sum_k N_{k,j}} (N_{i,j} - I_{i,j}) - \gamma I_{i,j}}_{\text{Transmission}} + \underbrace{r_{i,j} I_{i,i}}_{\text{Outbound}} - \underbrace{\tau_{i,j} I_{i,j}}_{\text{Inbound}}$$



Ross-Macdonald Equations

- Transmission among humans (X) is now driven through coupling to infectious mosquitoes (Z)

$$\frac{dX}{dt} = ba\frac{Z}{N}(N - X) - rX$$

$$\frac{dZ}{dt} = ac\frac{X}{N}(Me^{-gn} - Z) - gZ$$

- We can extend this model to incorporate movement, allowing humans to travel between many different locations. Each of those locations may have its own transmission intensity, defined by the local mosquito population

SIR + Movement Modeling

- Imagine instead modeling SIR-type dynamics across metapopulations connected by infrequent travel
- How does an SIR outbreak affect the residual population of susceptibles?
  - (Can calculate R0 this way)
  - Flux movement model homogenizes residual population sizes across all metapopulations
  - Time at Risk movement model preserves transmission heterogeneity
- Dynamics change as well
  - Flux movement model allows for oscillations, caused by back-filling of susceptibles in certain parameter regimes
  - Time at Risk movement model does not