Spatial Patterns of Falciparum Malaria Genetic Relatedness Driven by Human Movement in the Democratic Republic of the Congo

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Background on Relatedness

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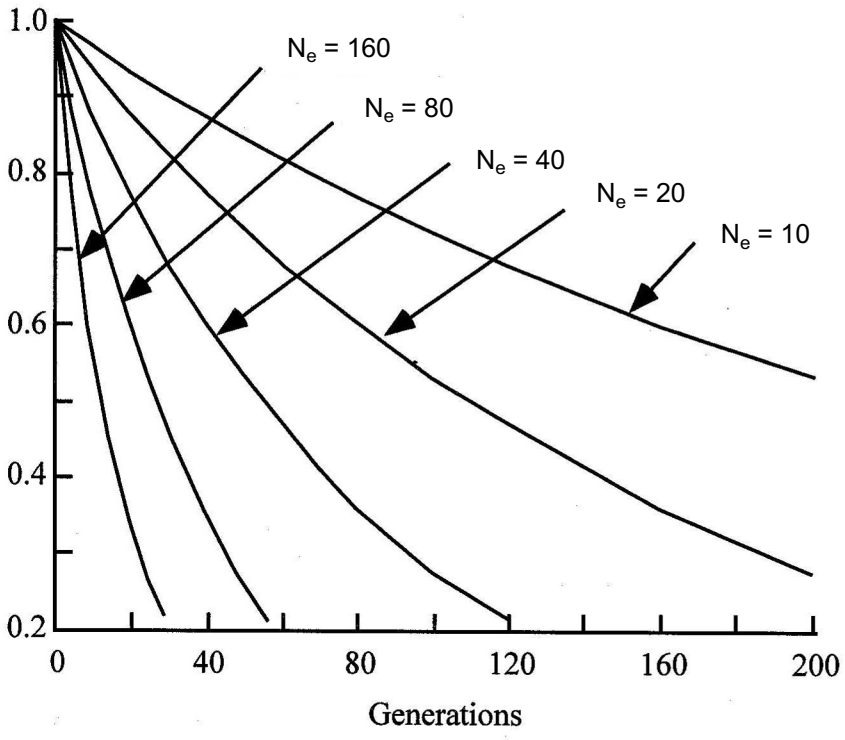
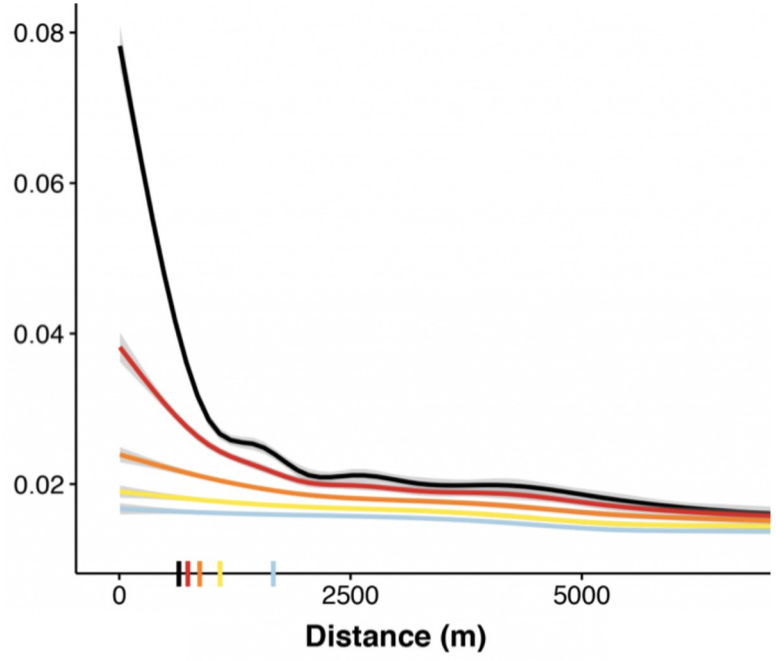
Population Size
(i.e. Inbreeding, Genetic Drift)



Wright, 1931
Kimura, 1968

Isolation by Distance



Malécot, 1948/1973
Wright, 1931/1942

Identity by Descent

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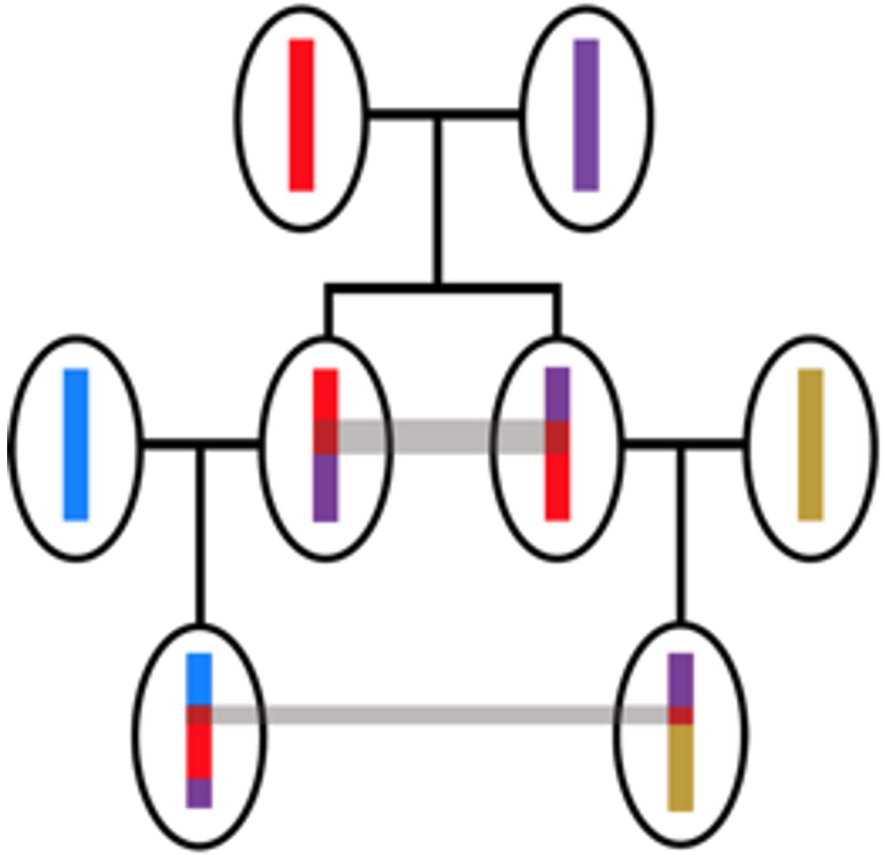

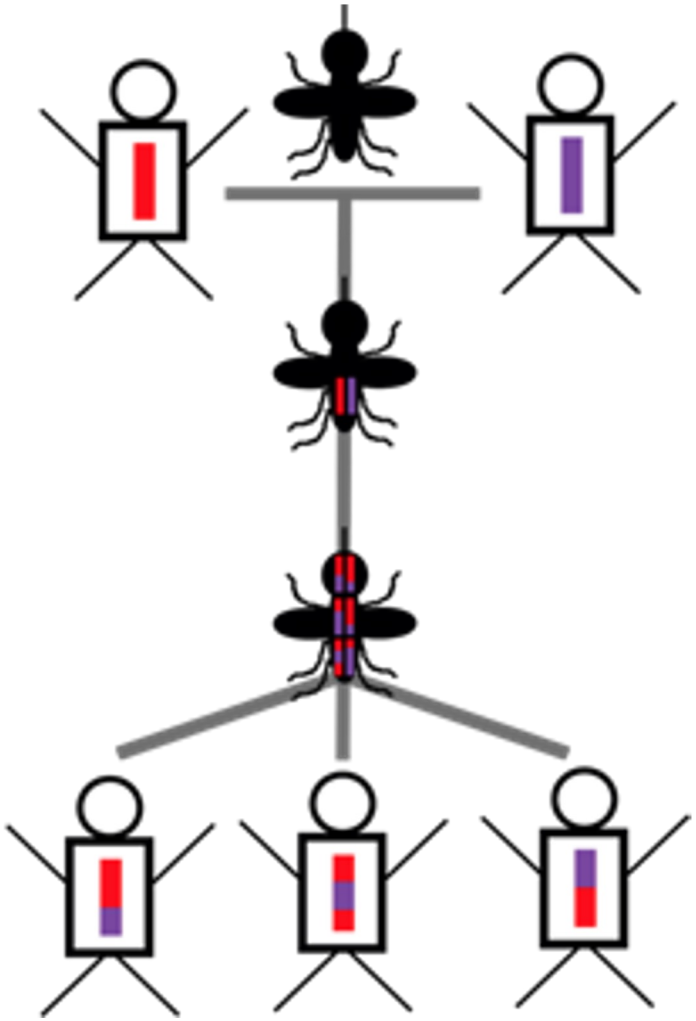

Identity by Descent

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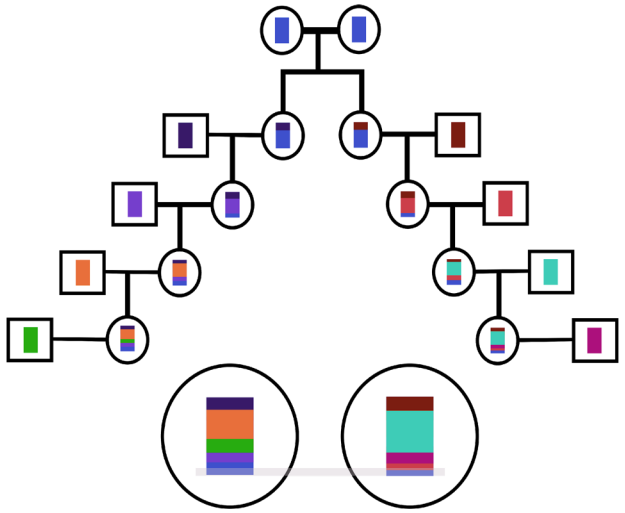

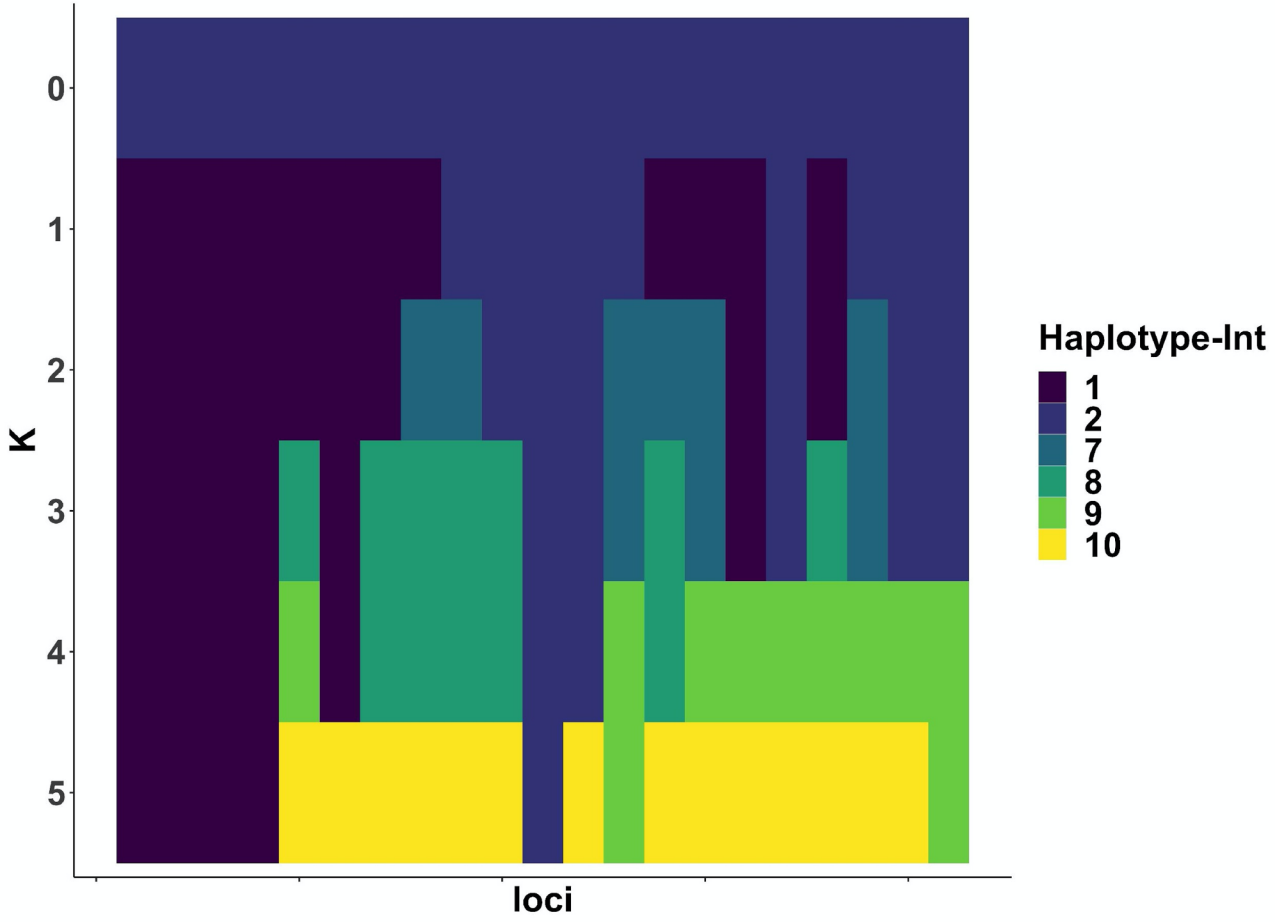

Strong, ephemeral signals

Identity by Descent (Malaria)

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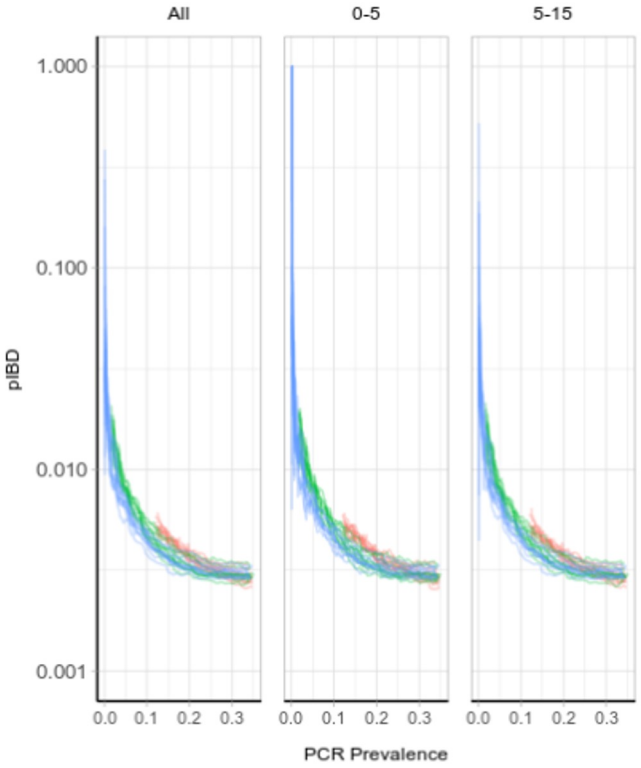
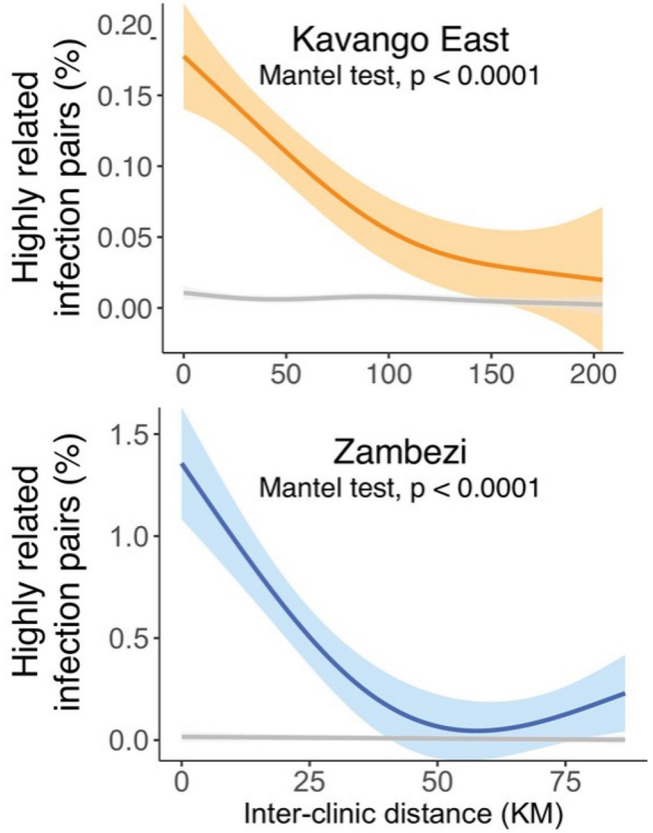
Population Size
(i.e. Inbreeding, Genetic Drift)



Watson *et al*., 2019 (BioRxiv)
Zhu *et al*., 2019, *ELife*

Isolation by Distance



Tessema *et al*., 2019, *Elife*
Chang *et al*., 2019, *ELife*

Identity by Descent (Malaria)

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Takeaway:

1. IBD is useful for public health
2. ***IBD reflects:***
    1. Transmission Intensity
    2. Spatial Patterns (isolation-by-distance)

Genomic Epidemiology DRC-DHS

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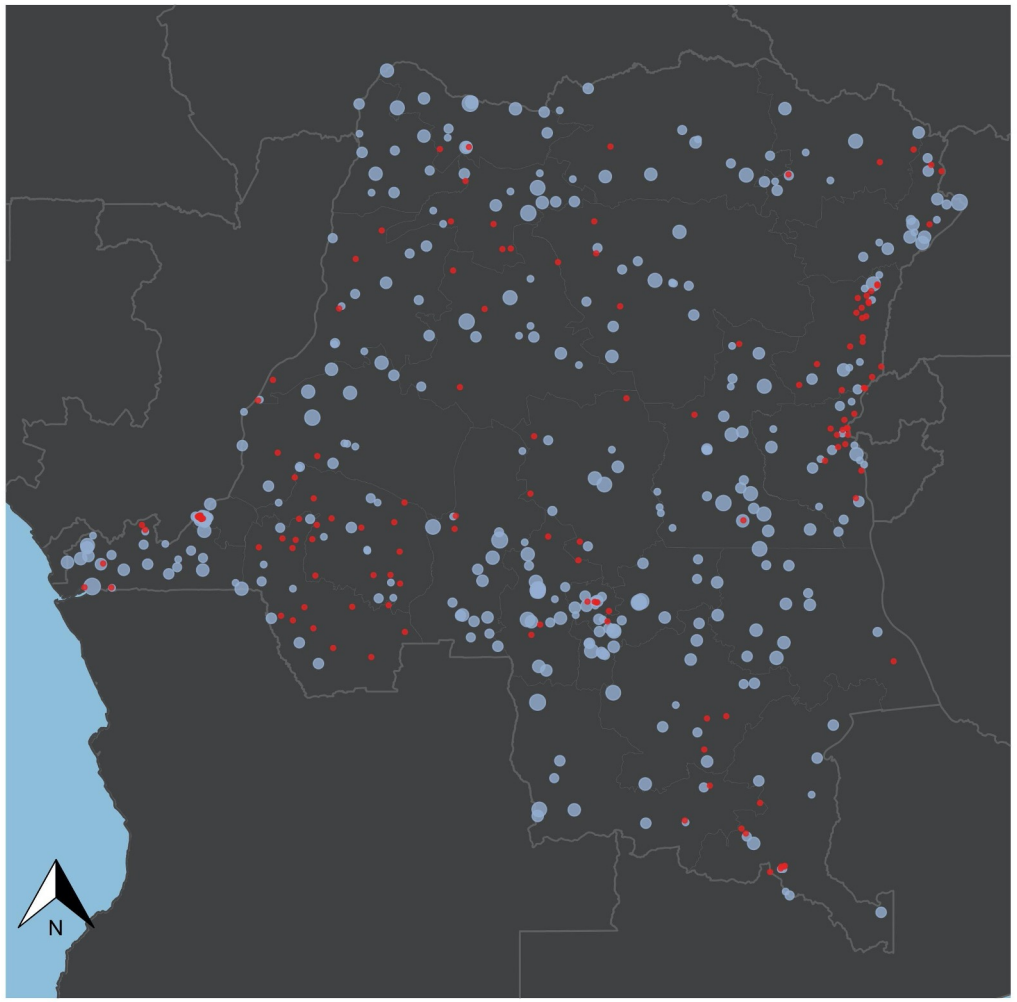

- **Falciparum Malaria in the DRC using the 2013-14 DHS**
- **1,111 isolates across 351/492 clusters in the CD2013**
  - » Cluster Size Range: 1 – 11 sequenced hosts
- **Genetic "Barcode"** (1,079 sites)

IDEEL @CAROLINA **Bailey & Juliano**

Genomic Epidemiology DRC-DHS

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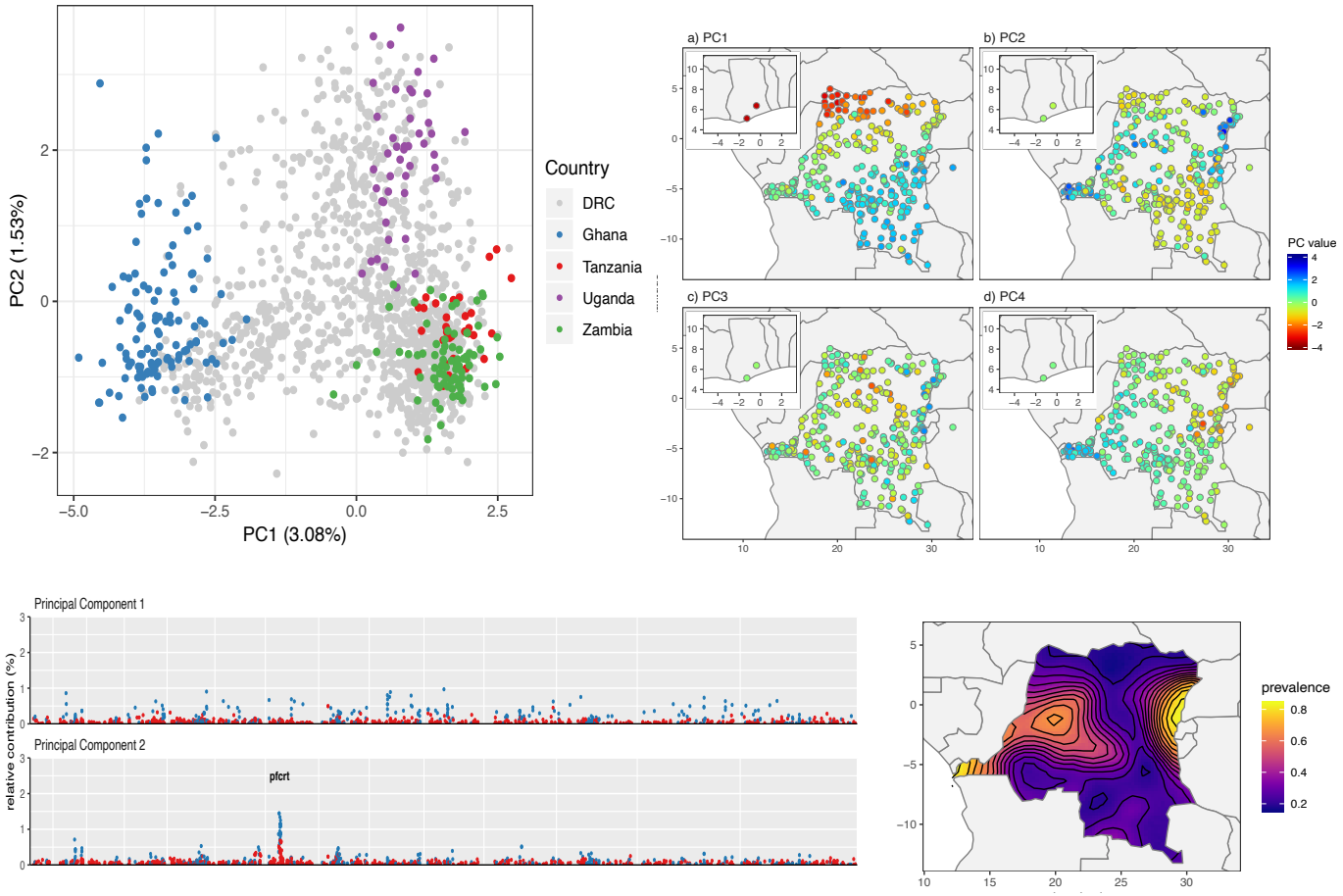

Takeaways:

1. High burden in DRC
2. Watershed region between East & West Africa
3. Genetic sub-structuring due to antimalarial resistance (“historic”)

Verity/Aydemir/Brazeau … Bailey/Juliano, Nat Comms 2020

Follow-Up Questions/Approach

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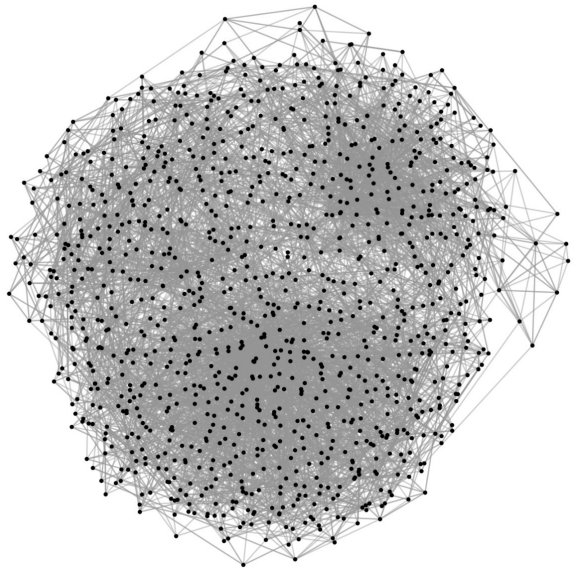
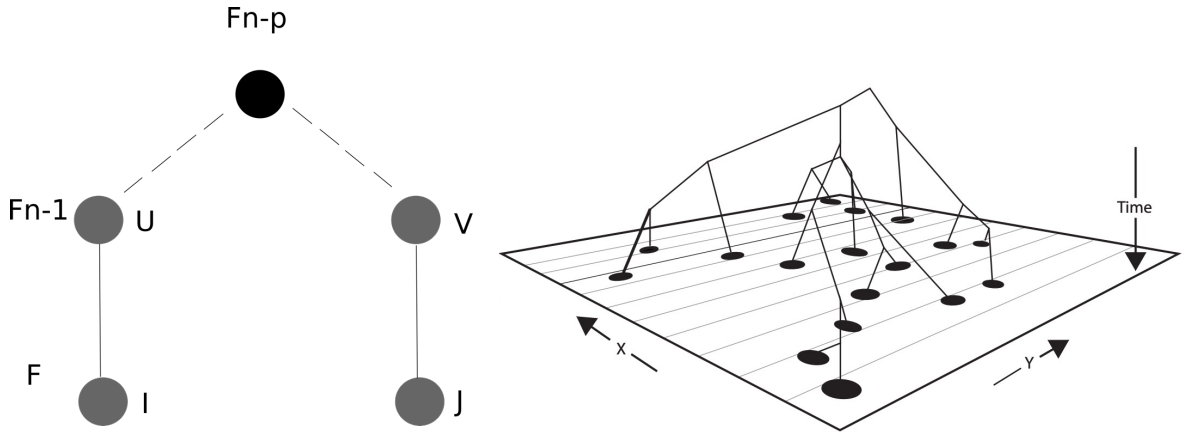
- **Can we leverage information on space to infer patterns of genetic relatedness and potentially transmission**



- **i.e. Can we find signal in this hairball?**

Deme Inbreeding Coefficient

$$r_{ij} = \left(\frac{f_i + f_j}{2}\right) exp\{-d_{ij}M\}$$



Based on Malécot, 1973

* Spatial coalescent figure from Battey *et al*., 2020 (ELife)

Oh, the places you'll go!

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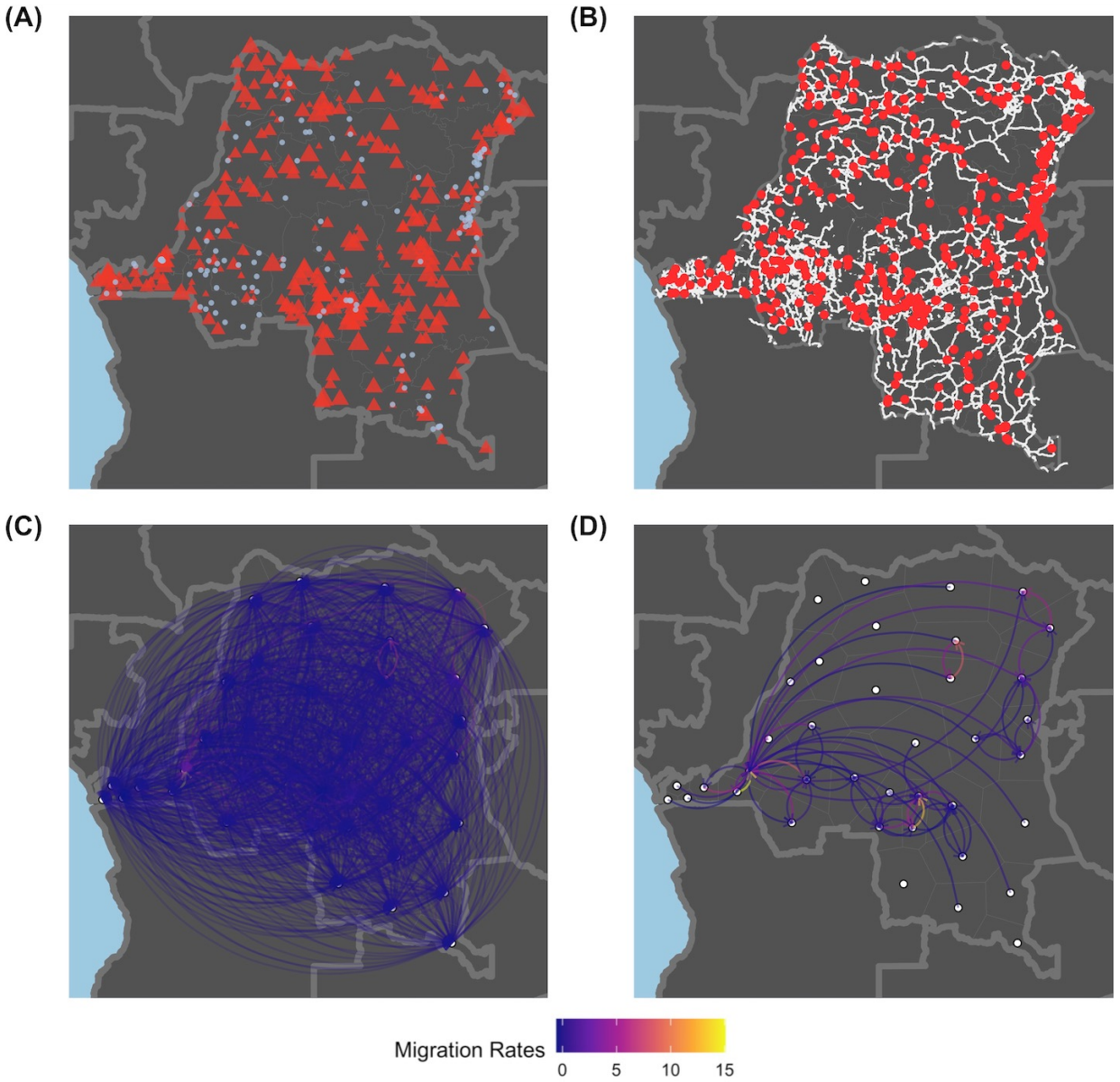

Space	Disperser
Greater Circle (A)	Mosquito
Roads (B) *Open Street Map*	Human
Migration Rates (C-D) *WorldPop*	Human

Spatial Modeling

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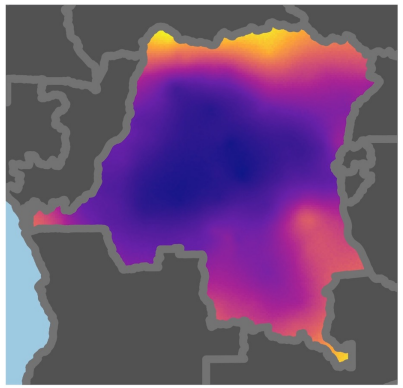

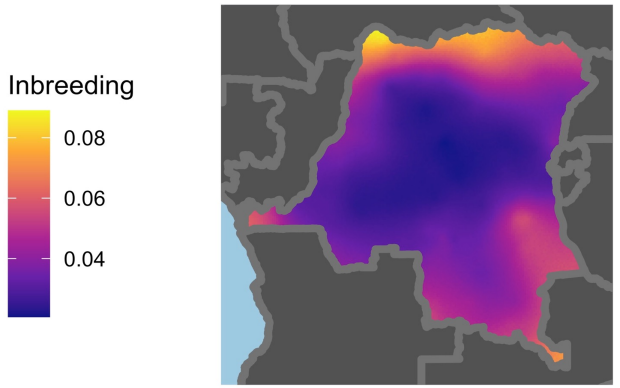

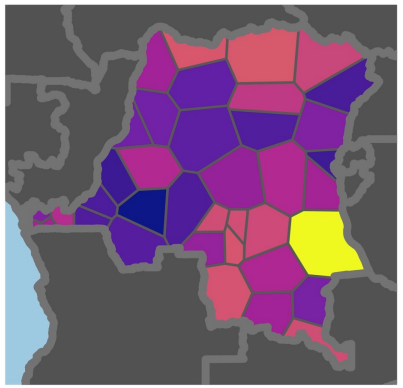

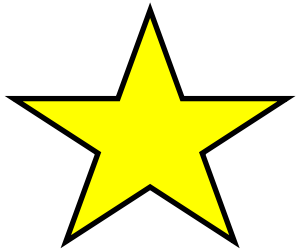

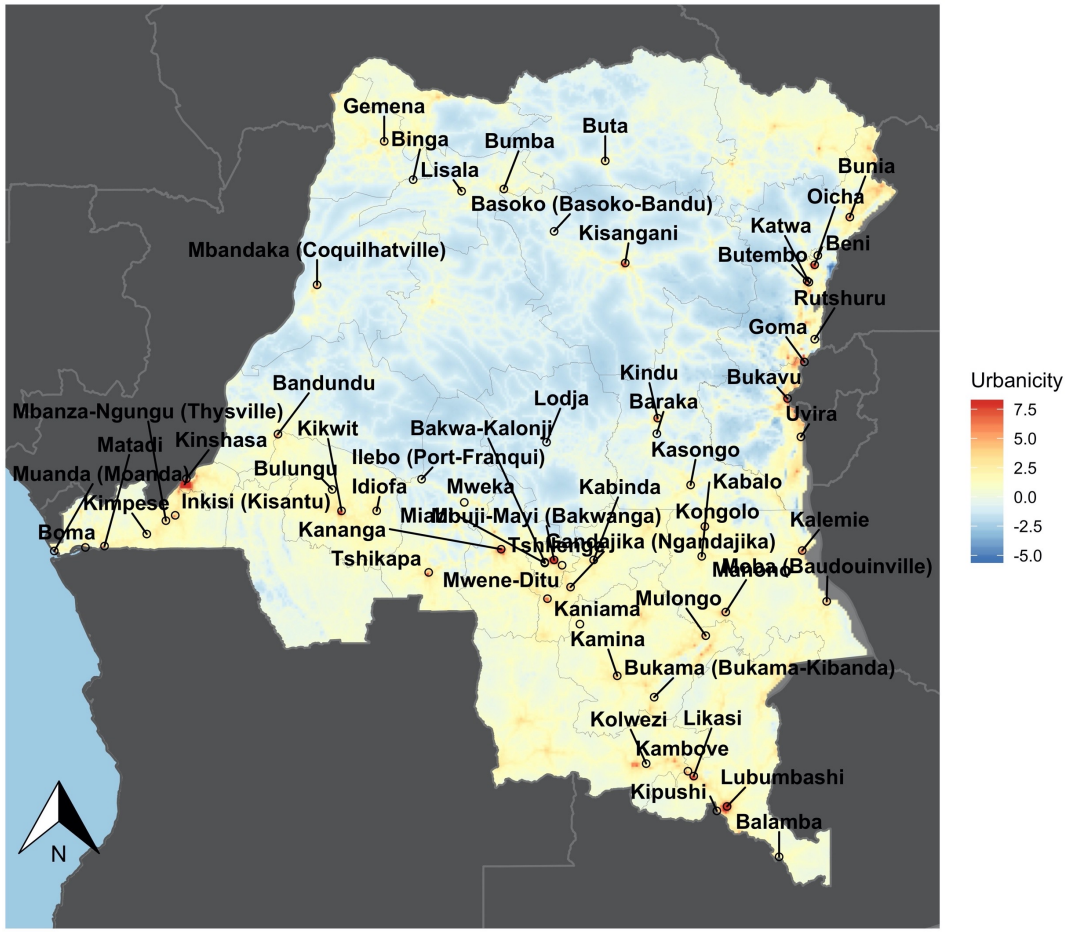

Community Detection Algorithms

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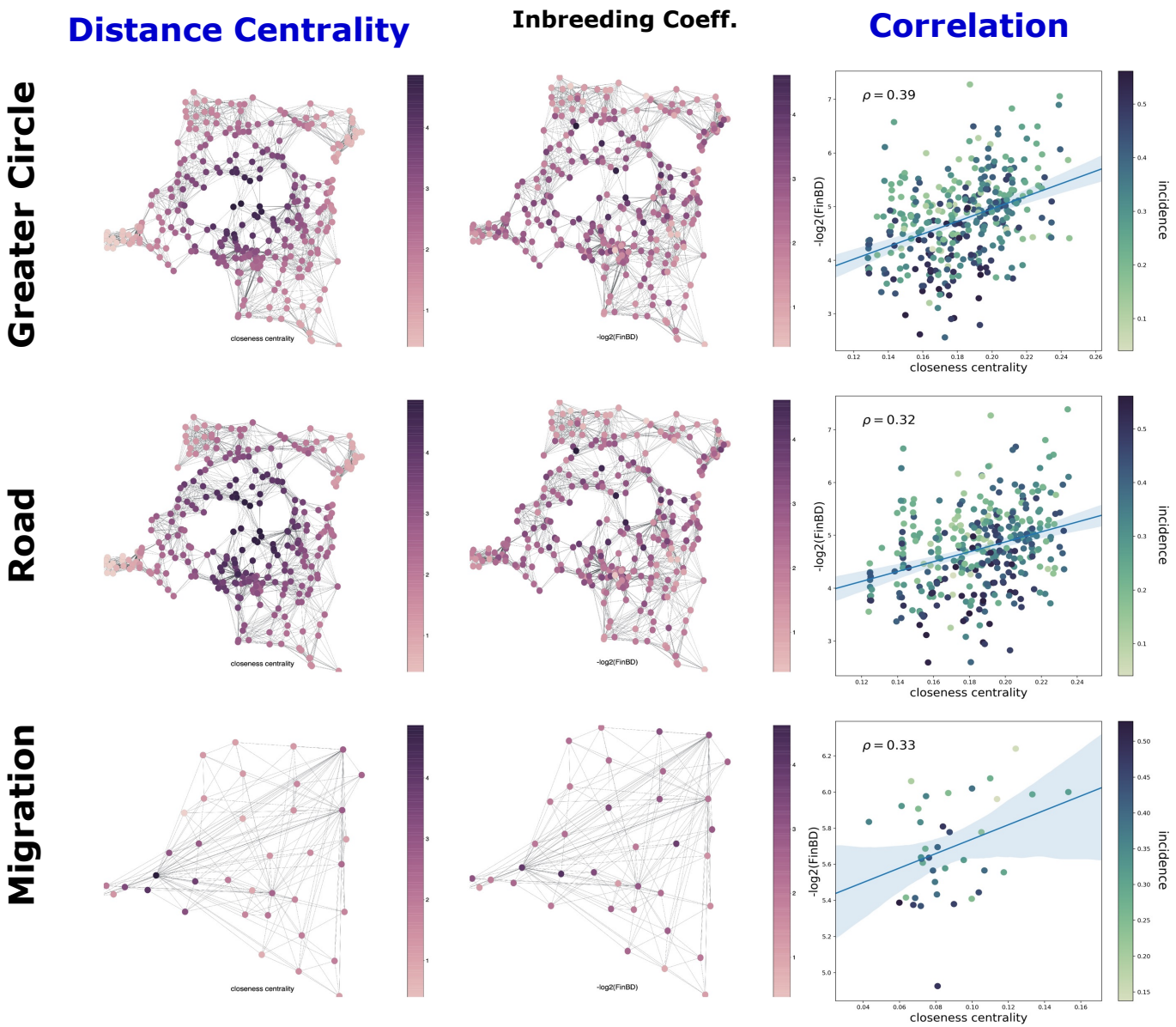
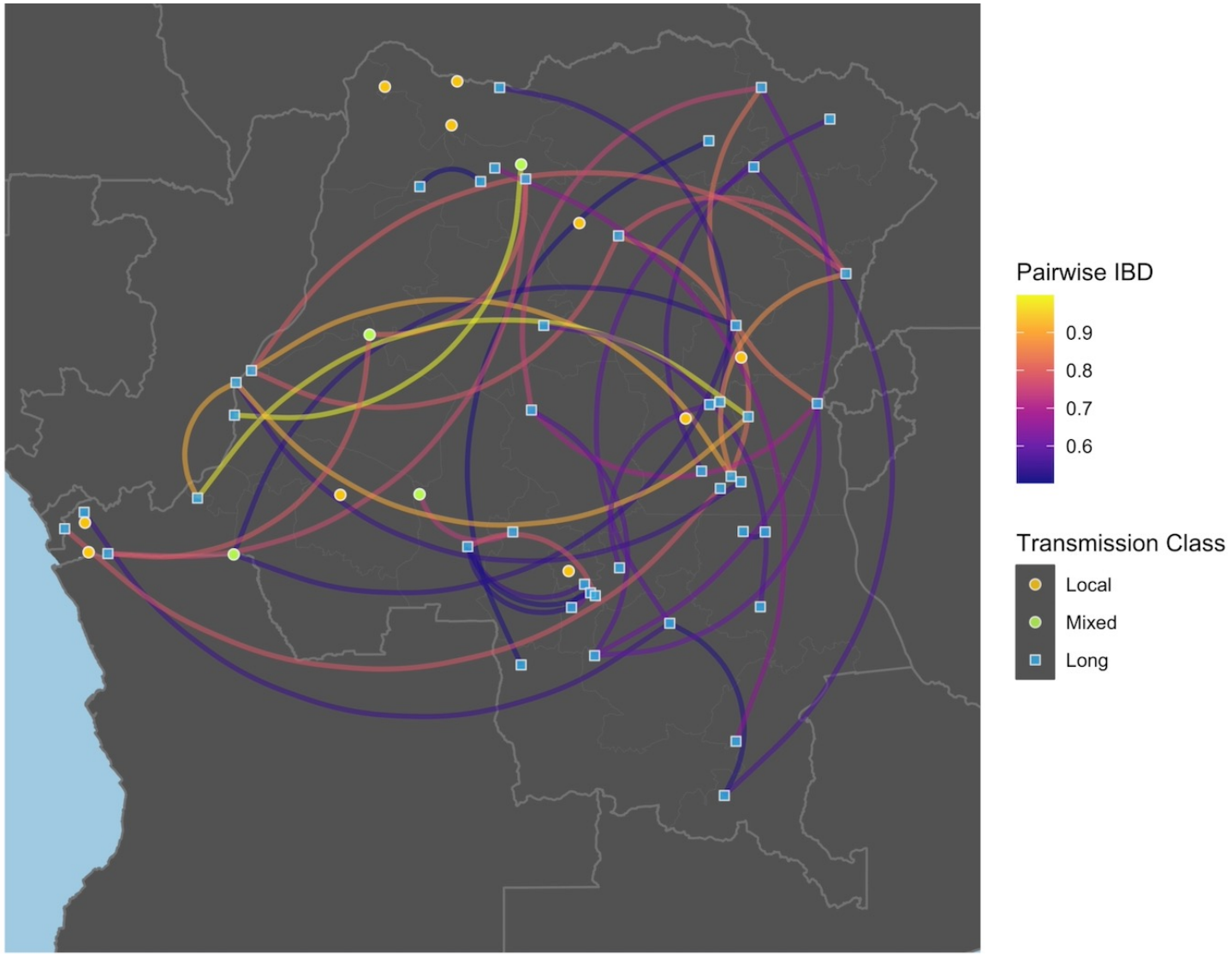


Community detection algorithms reveal that more central locations have less inbreeding

Highly Related Pairs



- Connections exceed expected mosquito flight lengths
- Transmission not limited to "local silos"

Minimum Road Distance: *50 km,* ***Minimum GC Distance:*** *25 km*

Diffusion Assumption

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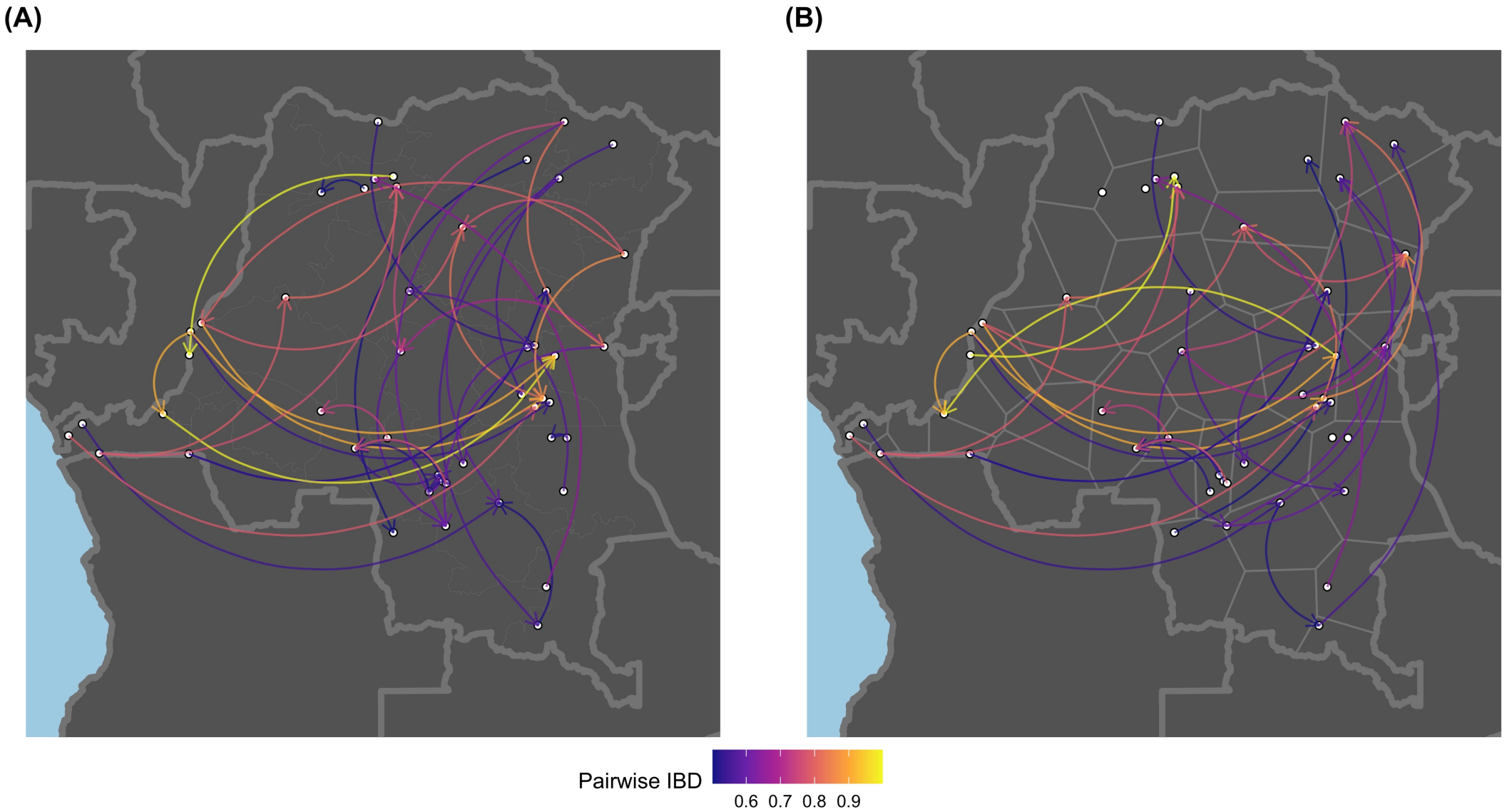
(Road) Genetic "Flow"



Migration "Flow"

Limitations & Conclusions

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Limitations:

1. Boundary effects
2. Mobility data (*e.g.* mobile phone data)
3. Relatedness measures and complexity of infection

Takeaways:

1. Human movement driving parasite dispersion in DRC
2. Cities are (likely) hubs

Relevance for Control:

1. Target hubs/Screen coming into hub
2. Understand gene flow in the DRC

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John Hopkins University

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- *Sophie Berube*

ASTMH

In Memoriam

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National Institute of Allergy and Infectious Diseases

Reproducibility & Data Availability

- *Analyses: nickbrazeau/Space_the_Final_Miptier*
- *Genetic Data: Upon Request*

GitHub

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