Kristan Schneider

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How often are you hit by an infection? - A likelihood approach to determine the multiplicity of infection

ROeS 2013, Sept. 12, 2013

What is malaria?

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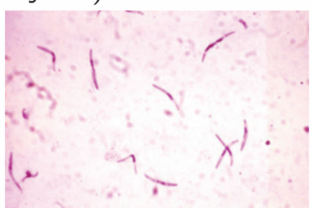
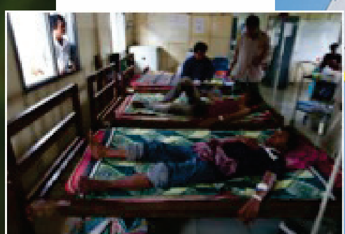
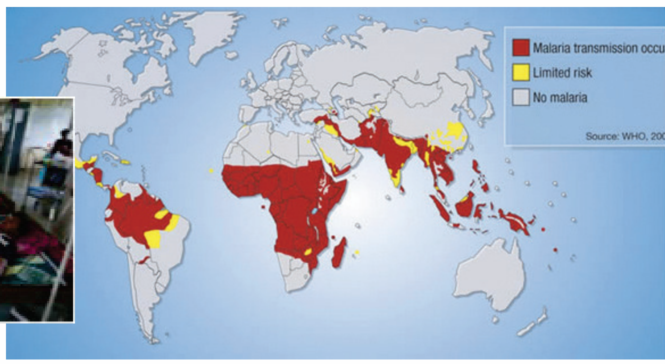
- Infectious disease caused by **parasites** (genus ***Plasmodium***; eukaryote)

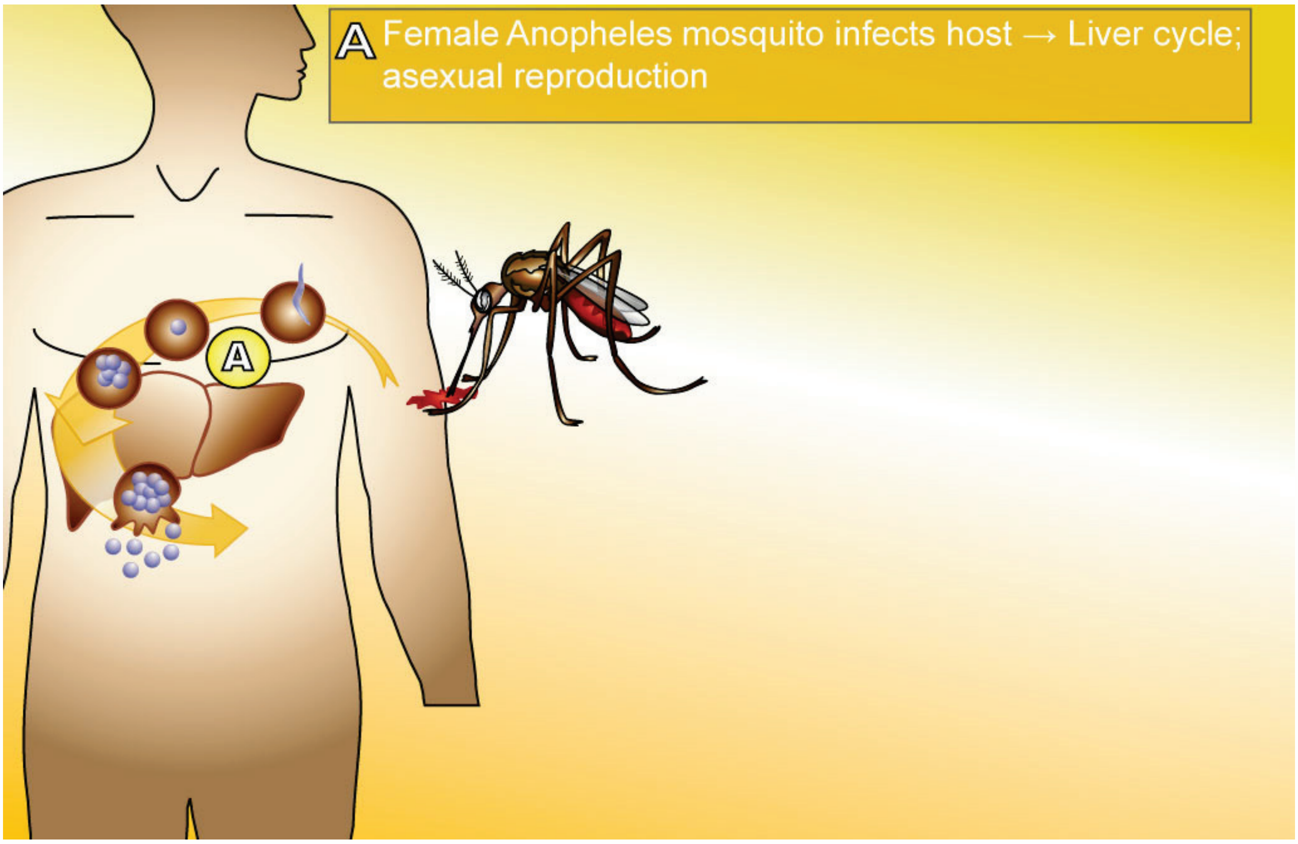


- 40% of the world's population at malaria risk
- Worldwide 200 - 300 million infections & 1-3 million deaths per year
- Enormous economic damage every year





Transmission cycle



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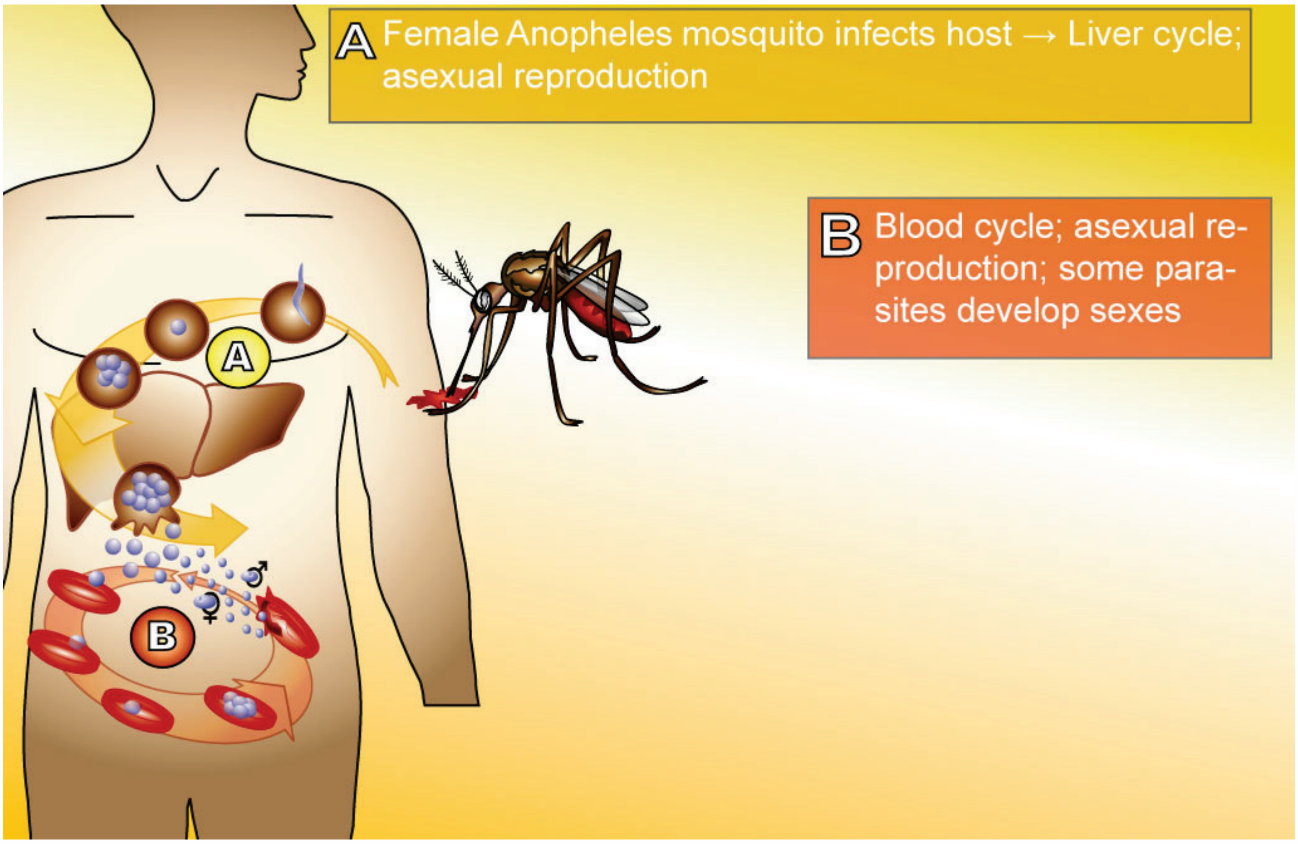

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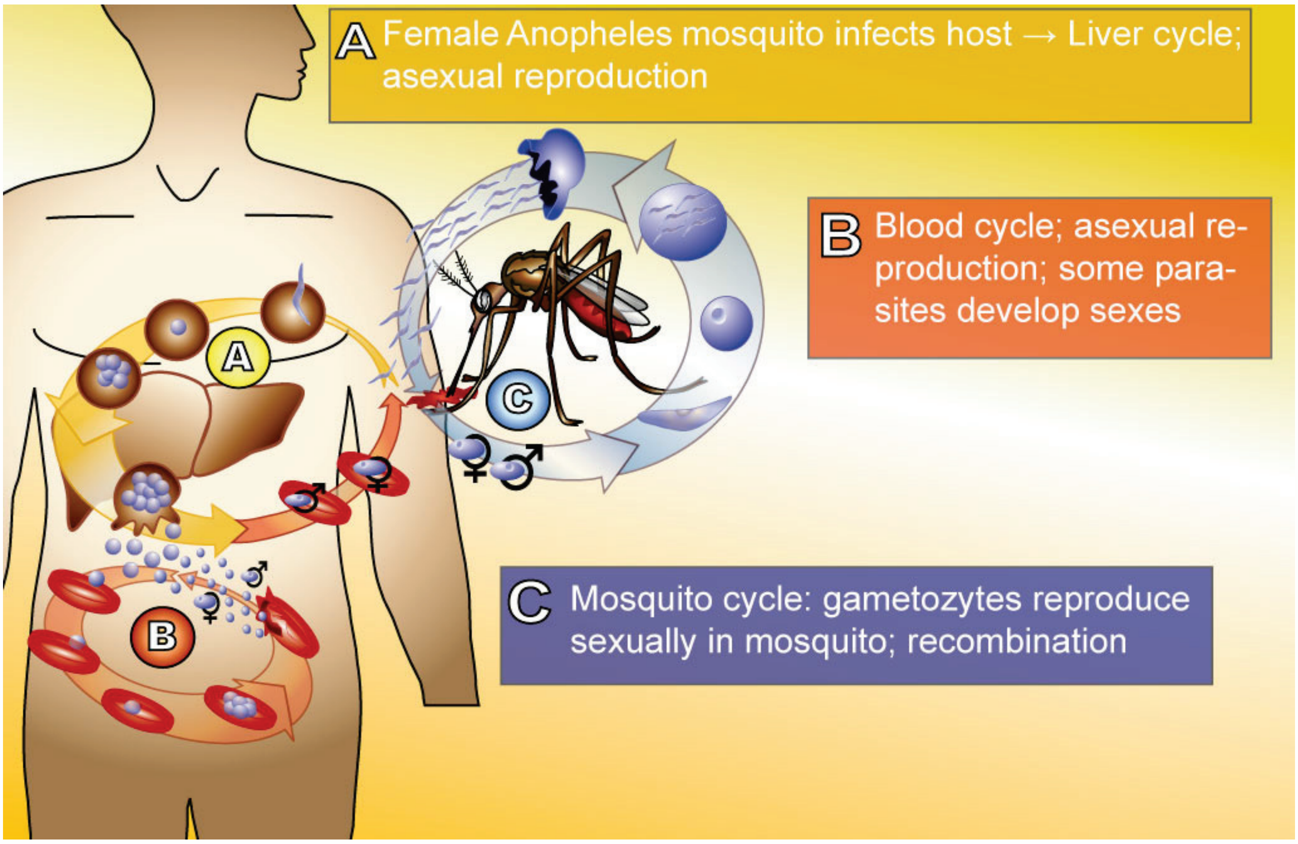

Malaria control

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Multiplicity of infection - Why is it important?

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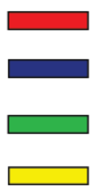

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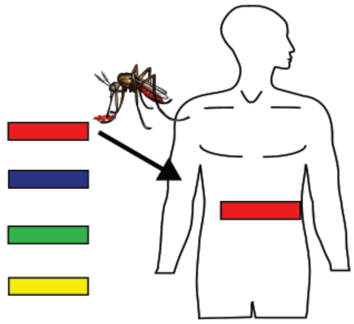

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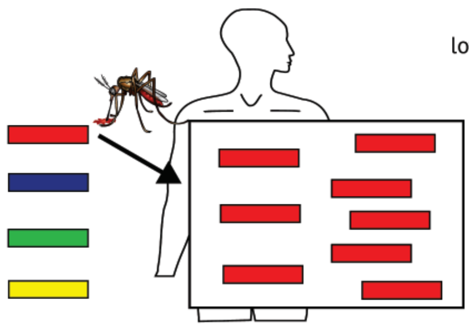

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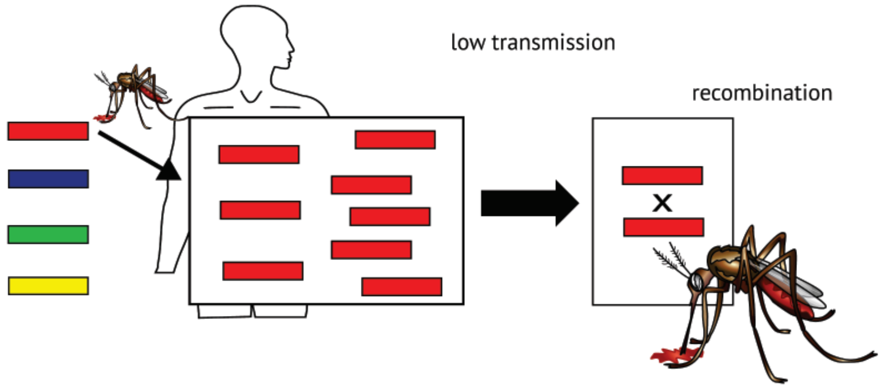

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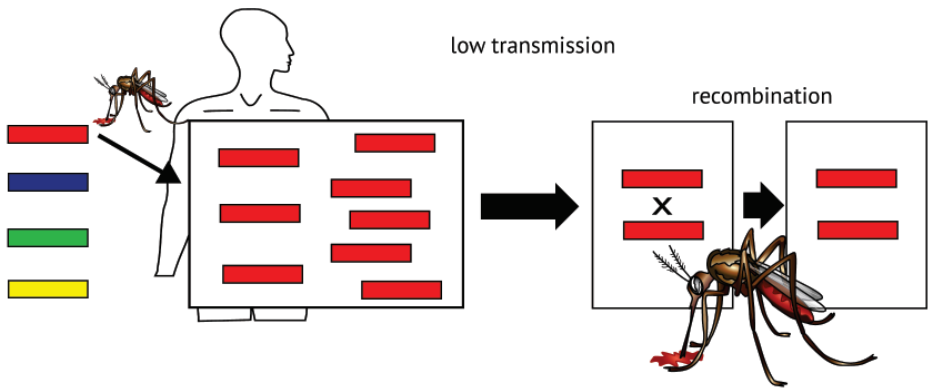

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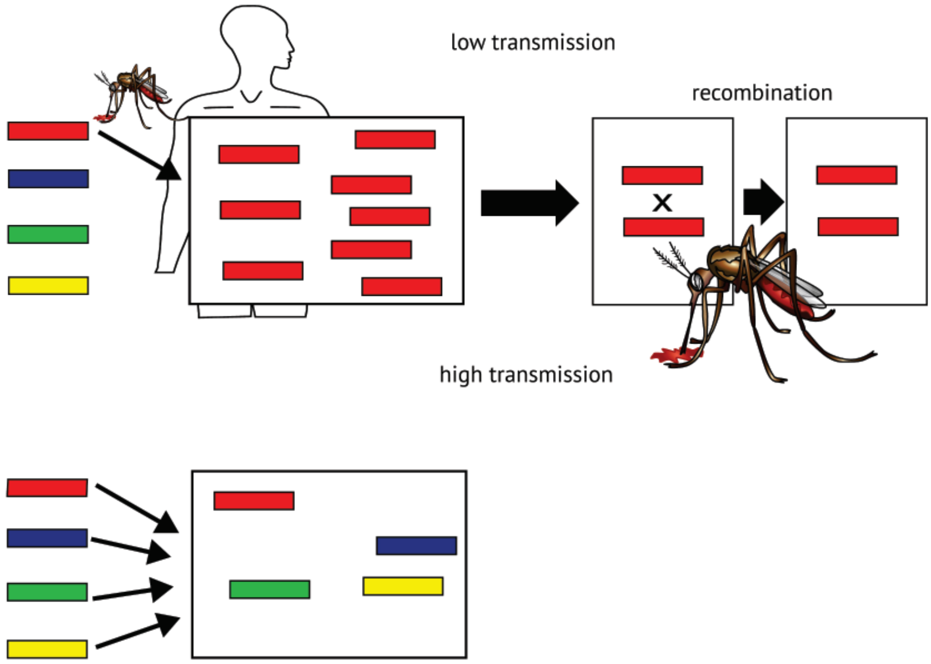

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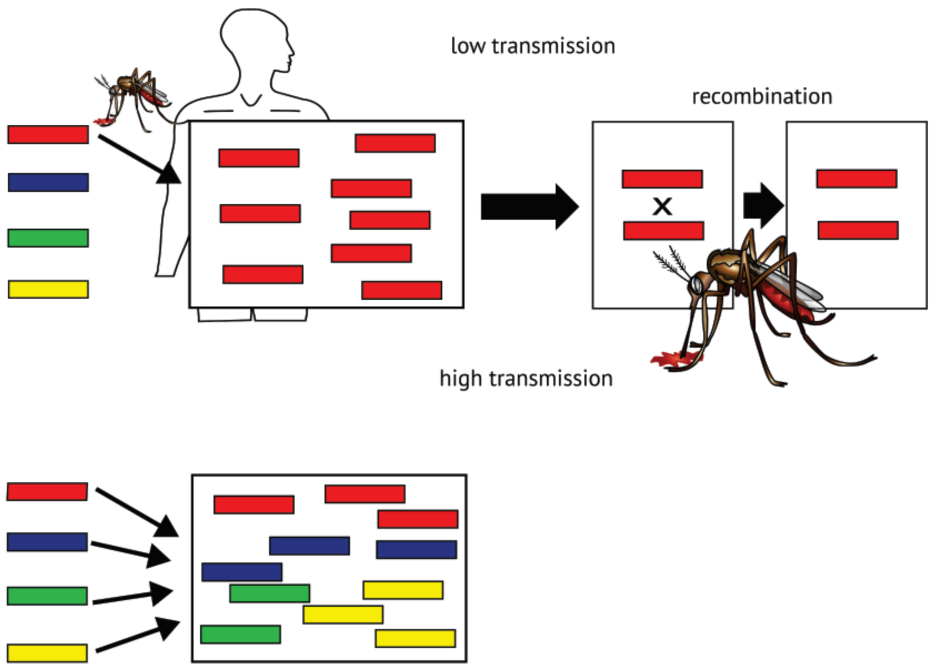

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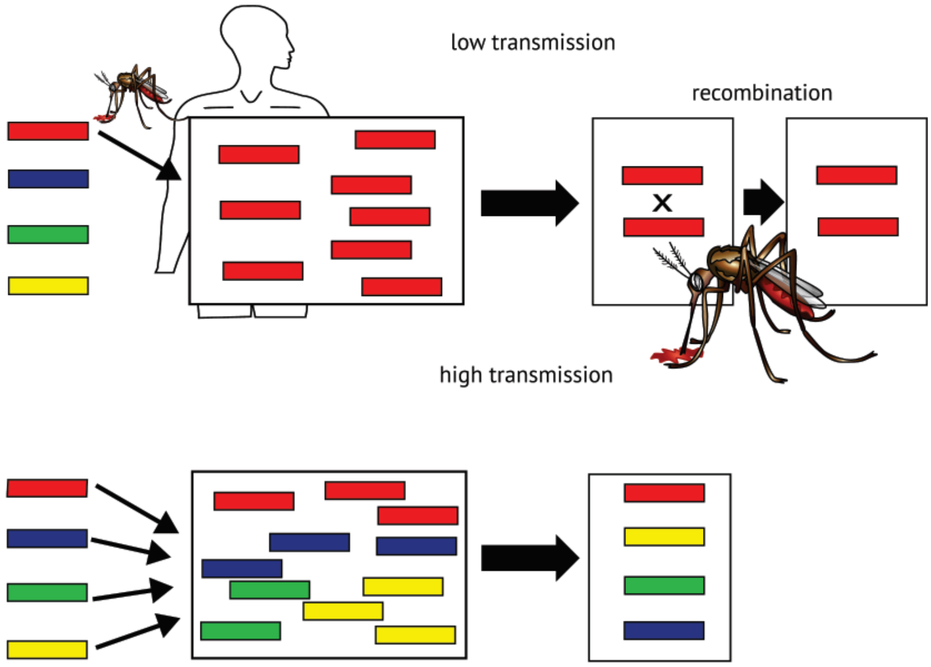

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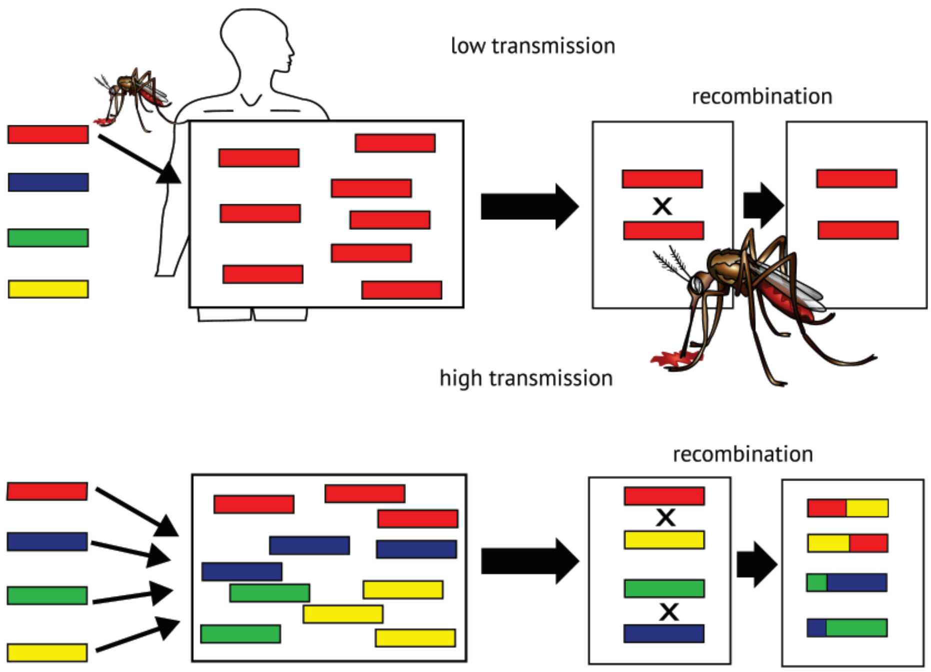

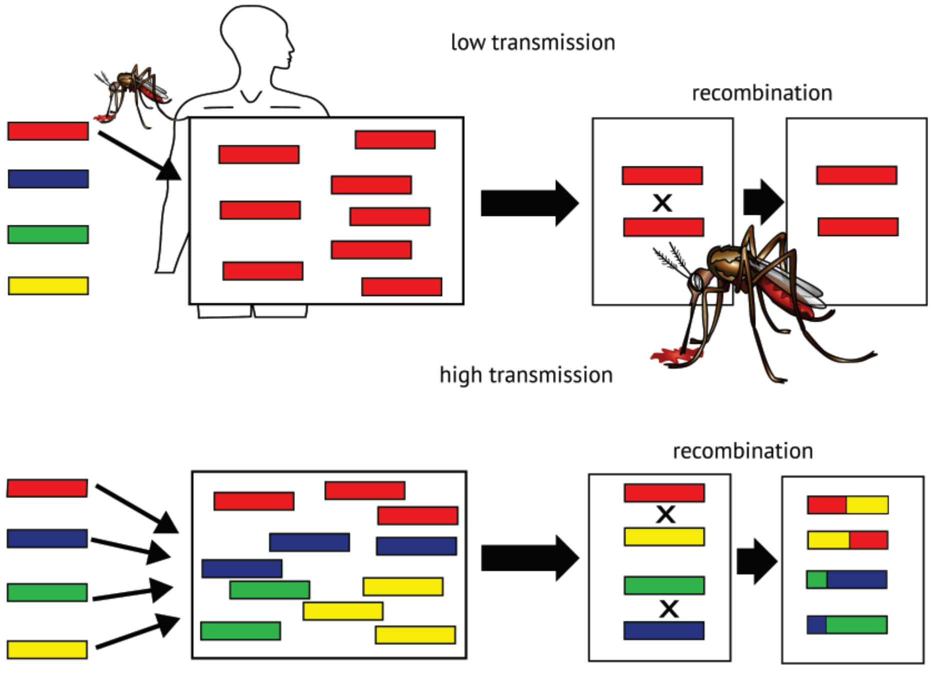

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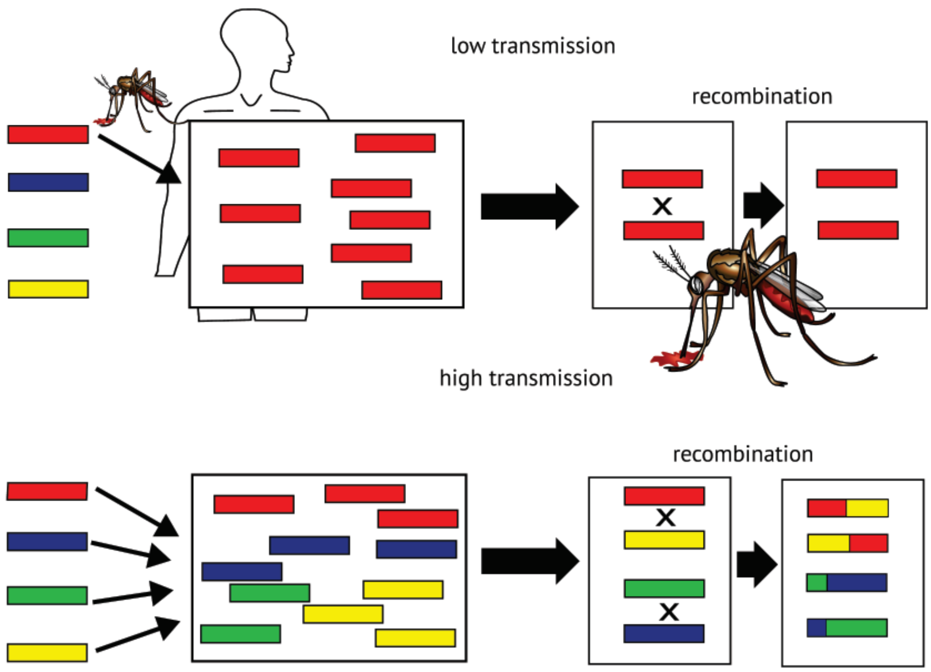
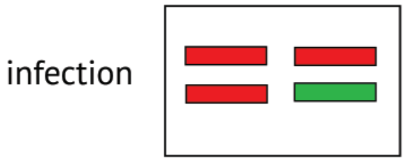


- Large number of co-infections = high transmission
- High transmission = more genetic variation

  → Multiplicity of infection = key quantity in genetic studies

Approach



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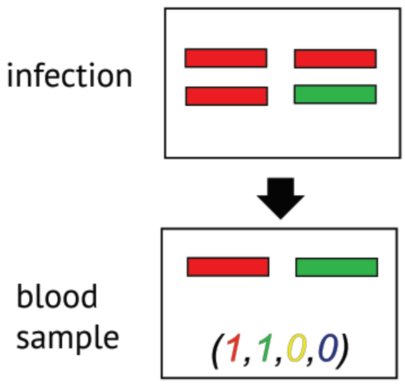

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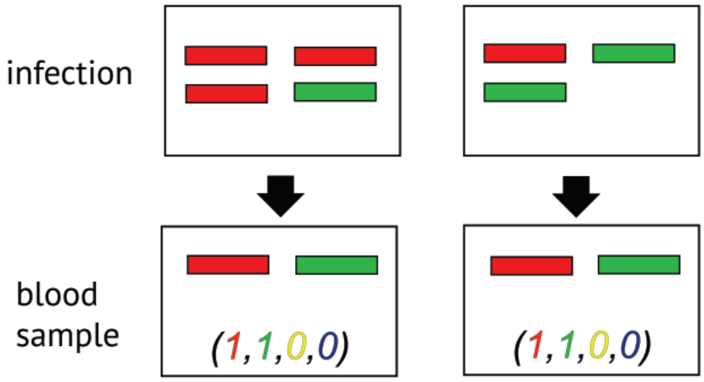

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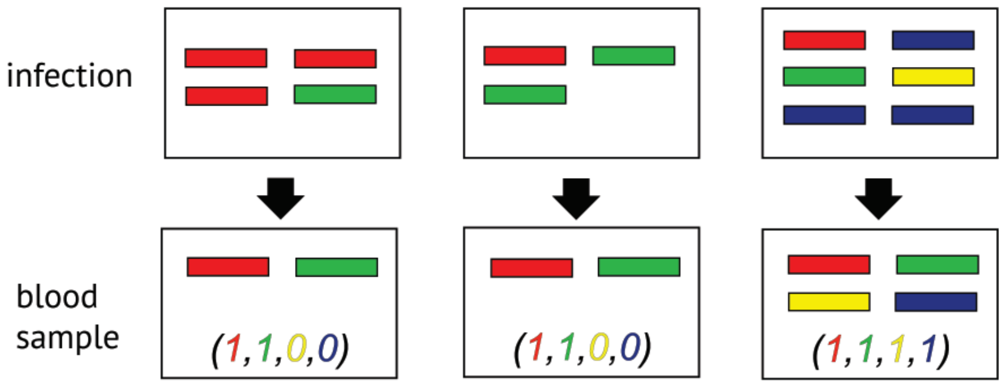

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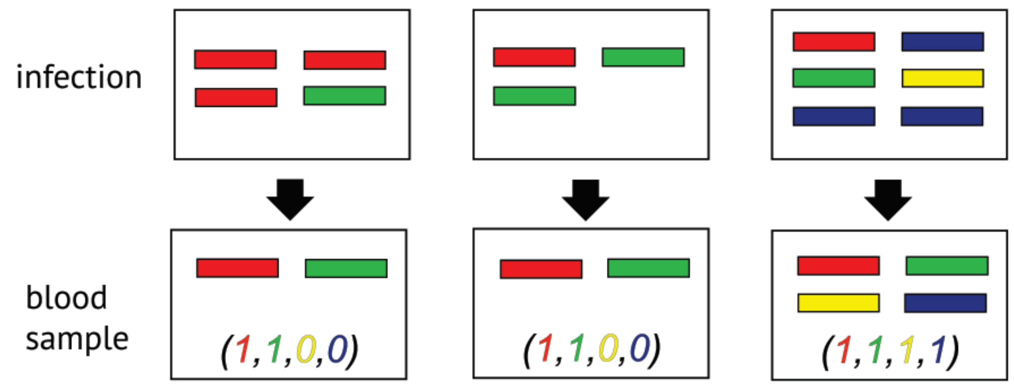

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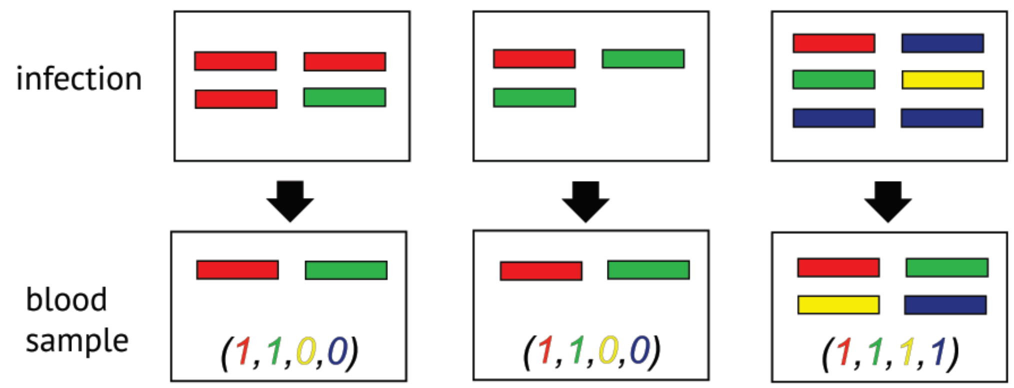

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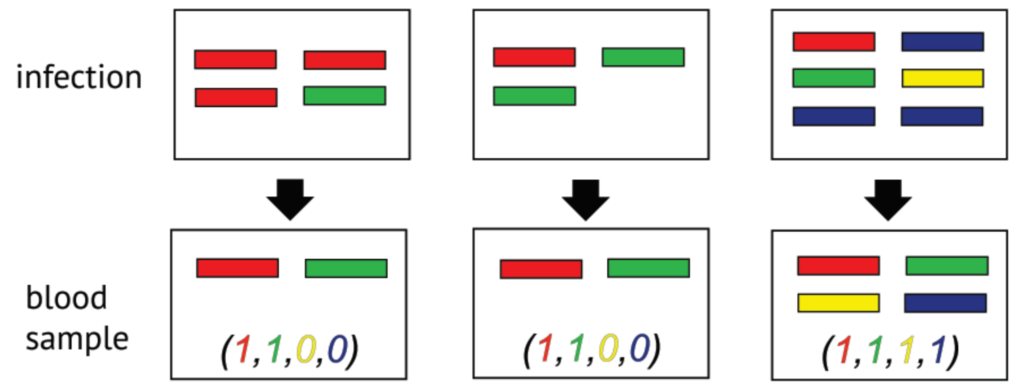

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Likelihood: $\prod_i Q_i^{n_i}$ Log-likelihood: $L = \sum_i n_i \log Q_i$

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  - Likelihood: $L = L(\lambda, \boldsymbol{p}) = -N \log(e^\lambda - 1) + \sum_{k=1}^{n} N_k \log(e^{\lambda p_k} - 1)$
  - $N_k \ldots$ number of samples with strain k

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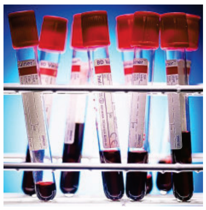

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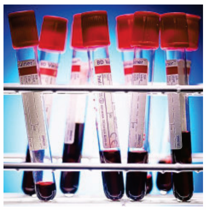
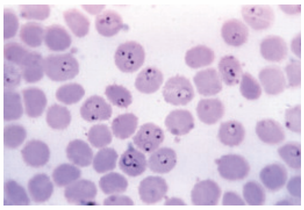

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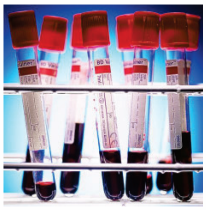
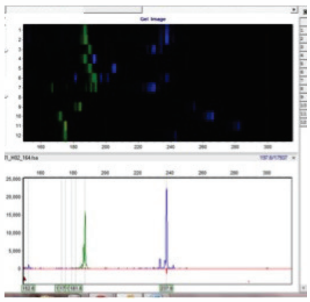
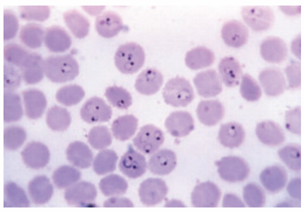

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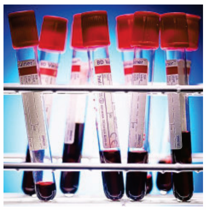
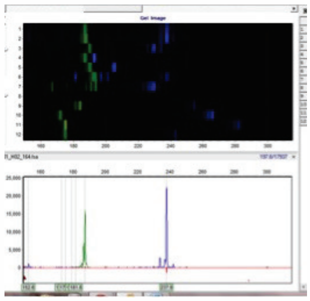
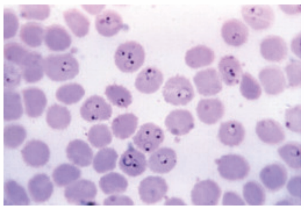


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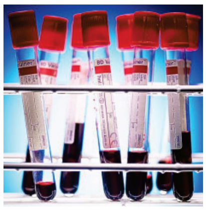
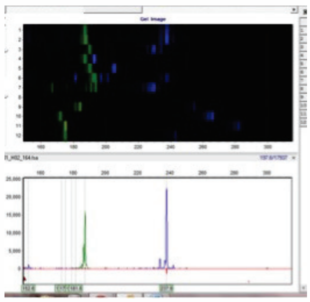
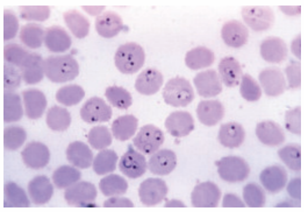


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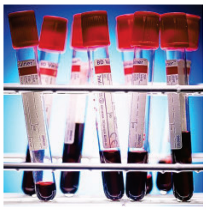

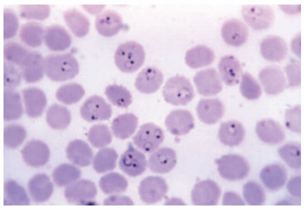

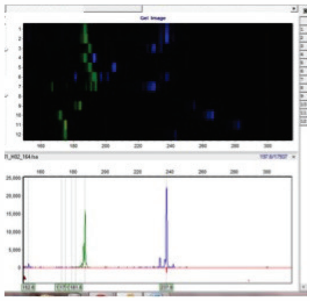

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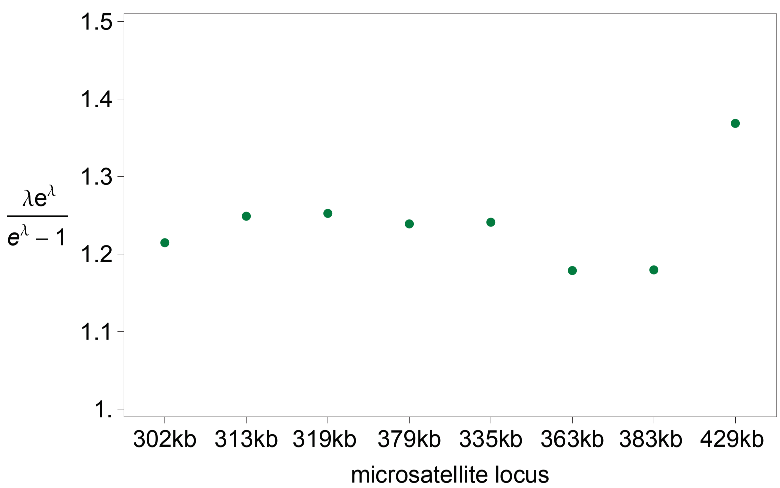

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Results

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- Aims:
  - Confidence intervalls
  - Testing the estimates
- Approach: **Profile Likelihood**
  - λ fixed $\quad L(\lambda, \boldsymbol{p}) \to \max$?
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  - Trick: maximize conditioned on $L(\lambda, \boldsymbol{p}) = \ell^*$

    $\to$ Lagrange multiplies & (n+1)-dimensional Newton method

Results:

- $1 - \alpha$ confidence intervals exist & uniquely defined

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  reject H_0 if $\lambda_0 \notin [\underline{\lambda}, \overline{\lambda}]$

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  $$\chi_1^2\Big(2(\max_{\lambda,\boldsymbol{p}} L(\lambda,\boldsymbol{p}) - \max_{\boldsymbol{p}} L(\lambda_0,\boldsymbol{p}))\Big)$$

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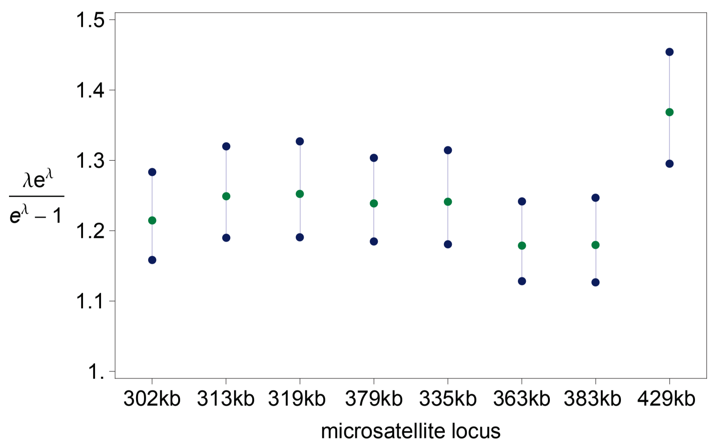

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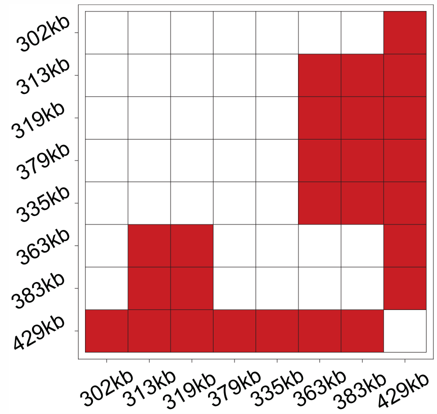
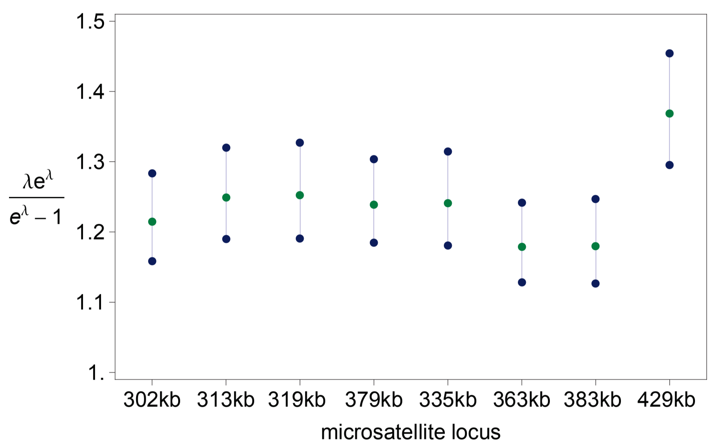
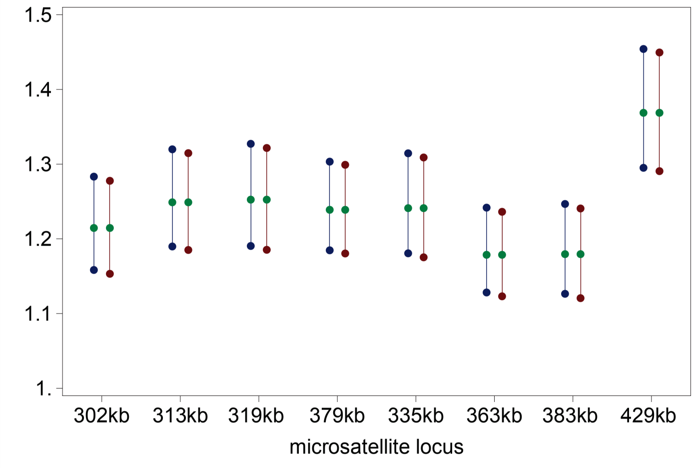
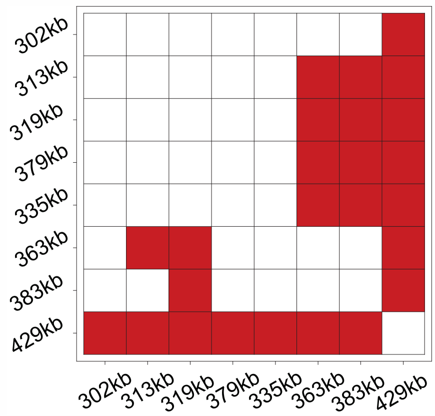


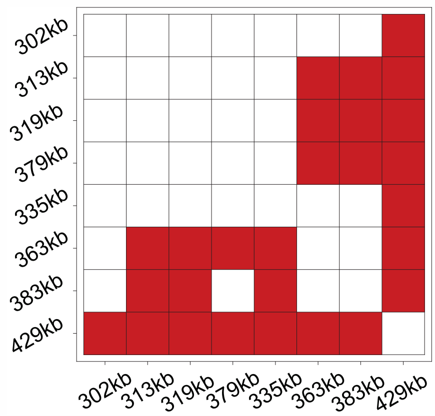


Results

$$(\hat{\boldsymbol{\theta}} - \boldsymbol{\theta}_0) \sim \mathcal{N}(\mathbf{0}, I_N^{-1}(\boldsymbol{\theta}_0))$$







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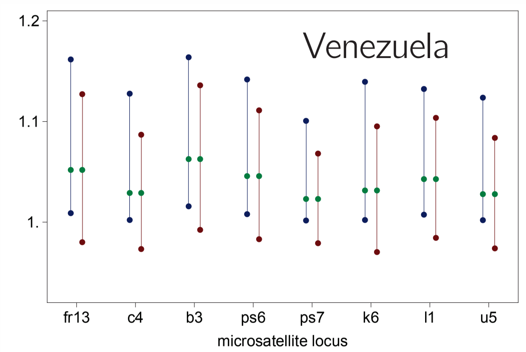

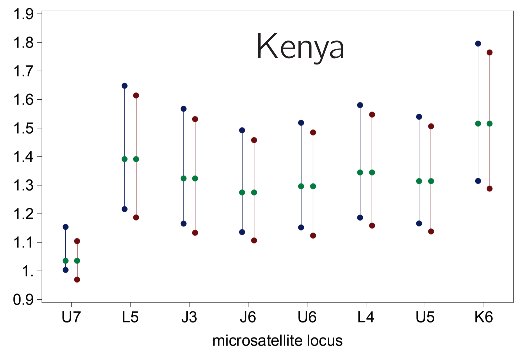

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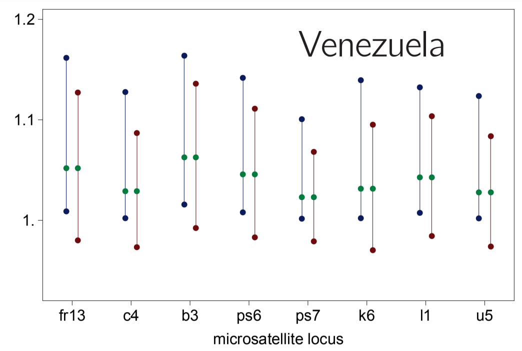

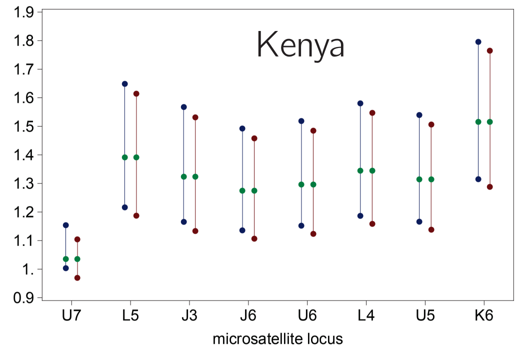

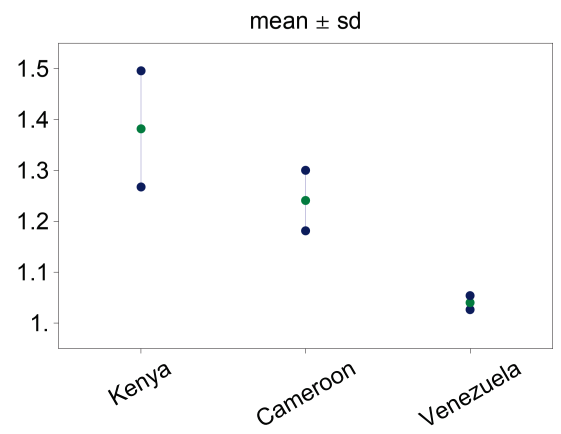

Conclusions

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- ML estimate for number of co-infections

  (key parameter in malaria)

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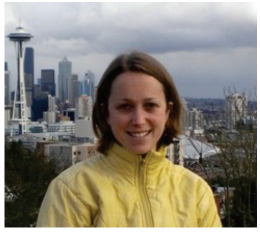

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