

Which Phenotypes Affect Bacteria's Inhibition Ability?

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Who and When

- Summer of 2014, consulting project through School of Statistics consulting clinic

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- Linda Kinkel: Department of Plant Pathology
- Cheng Zhang
- Yang Yang
- Aaron Renhdal

What

- Bacteria can produce antibiotics



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- Our research subject:
streptomyces



What

- Bacteria can produce antibiotics
- Our research subject:
streptomyces
- How does location, genetic similarity and niche overlap affect *streptomyces*'s inhibitory ability?



Why

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- Streptomycin was the first cure for tuberculosis
- The mechanism of antibiotics production remains unanswered

The Data

- Global data: 83 different *Streptomyces* isolates, 7 locations around the world

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- We were not involved in data collection nor designing experiment

Response Variable: Size of the Killing Zone

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- Need to do $P_2^{83} = 6806$ experiments!

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- Example: A uses 40 units of nutrients in total, B uses 20 units of nutrients in total, 10 units of nutrients are overlapping. Then niche overlap for A is: 25%, for B is 50%
- We wrote R function to calculate the niche overlap from raw data and store the values in a square matrix (NOT symmetric)

Predictor Variable: Genetic Distance

- Between 0-1
- Measures the similarity between the genes of two isolates
- Calculated by Biology Workbench
- Stored as a symmetric matrix

Predictor Variable: Locations

- Locations were treated as factors

Preliminary Work

- Clients claim that they have found significant correlation between “certain” predictors and response variable

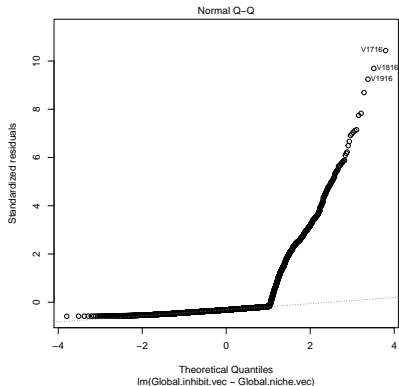
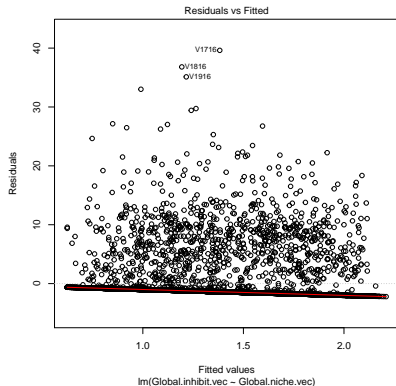
Preliminary Work

- Clients claim that they have found significant correlation between “certain” predictors and response variable
- We started with multiple linear regression, tried to reproduce clients' results

However...

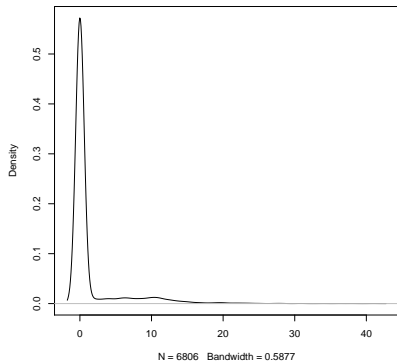
- We could not reproduce the same results
- Multiple regression did not fit the data well

Regression Diagnostics

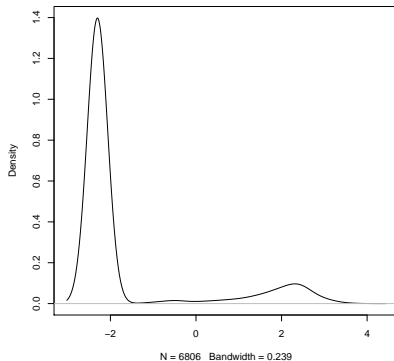


Zero Inflated Response

Density Plot



Density Plot after log transformation



83% of the response are zeros!

Inspiration: Auto Insurance Data

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- In auto insurance data, over 90% of the data does not have any claim. (response= 0)
- Zero Adjusted Inverse Gaussian (ZAIG) model has been well established

ZAIG in a nutshell

- Model the probability of killing and killing ability separately

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- Killing \sim Bernoulli($1, \pi$)
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- Mixed continuous-discrete distribution

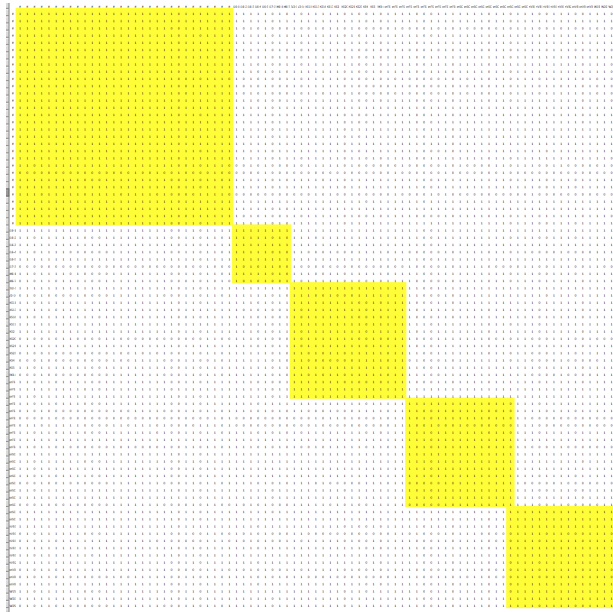
ZAIG in a nutshell

- Model the probability of killing and killing ability separately
- Killing \sim Bernoulli($1, \pi$)
- Size of killing zone \sim Inverse Gaussian(μ, σ)
- Mixed continuous-discrete distribution
- `library(gamlss)`

Sympatric Analysis

- Clients specifically asked for two models
- Sympatric: intra-location
- Allopatric: inter-location

Sympatric Analysis



Sympatric Analysis

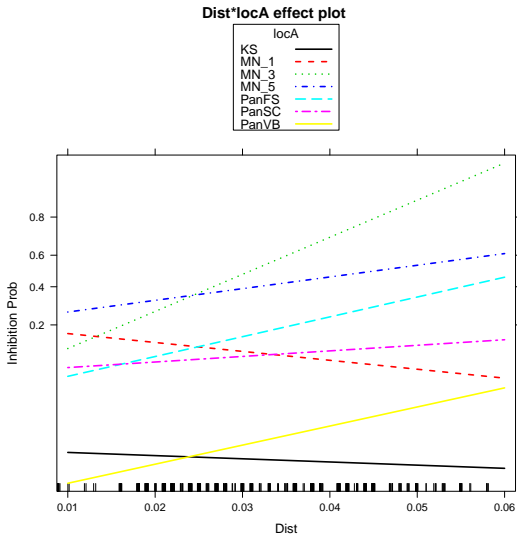


Figure : Interaction of Dist:locA

Sympatric Analysis

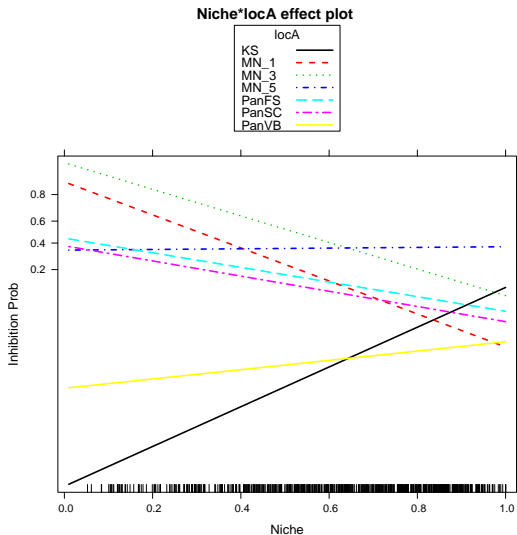
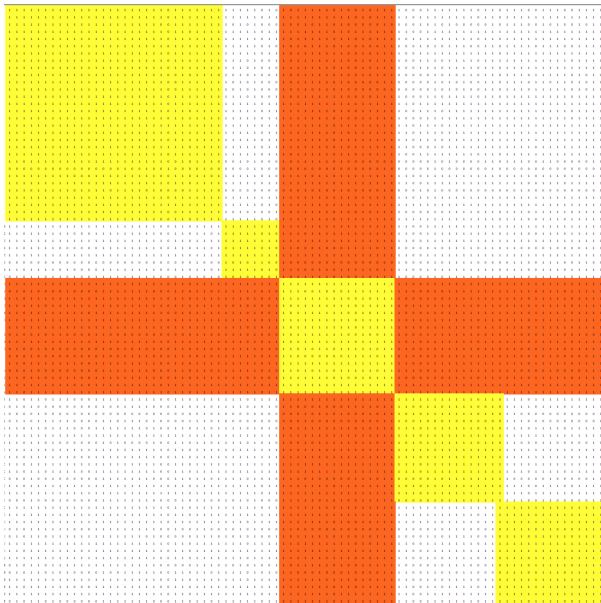


Figure : Interaction of Niche:locA

Allopatric Analysis



Allopatric Analysis: MN1

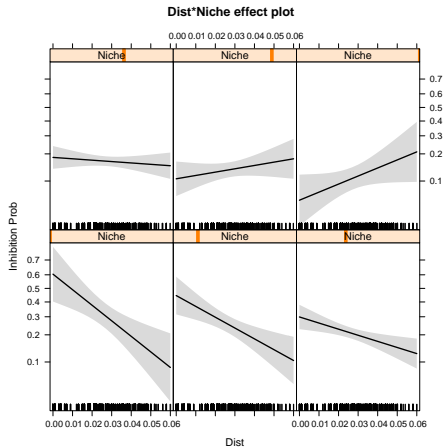


Figure : Interaction plot of Dist:Niche at MN1

- Inhibition size: none of the predictors are significant.

Allopatric Analysis: MN3

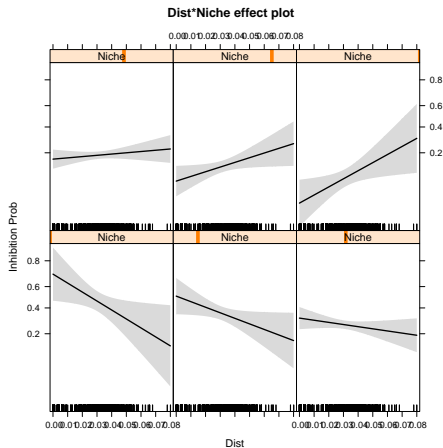


Figure : Interaction plot of Dist:Niche at MN3

- Inhibition size: genetic distance is significant ($p = 0.029$). The inhibition size increases 8.8% as the distance increases by 0.01 unit.

Allopatric Analysis: MN5

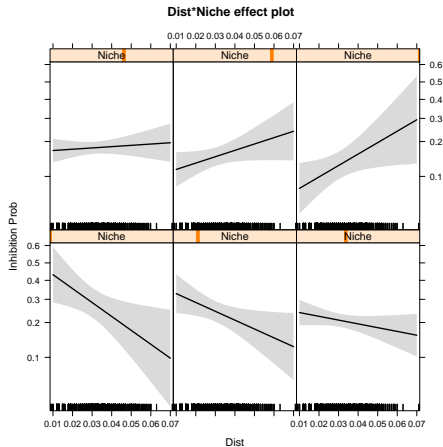


Figure : Interaction plot of Dist:Niche at MN5

- Inhibition size: none of the predictors are significant

Allopatric Analysis: Kansas

- Inhibition probability: none of the predictors are significant.
- Inhibition size: none of the predictors are significant.

Allopatric Analysis: PanFS

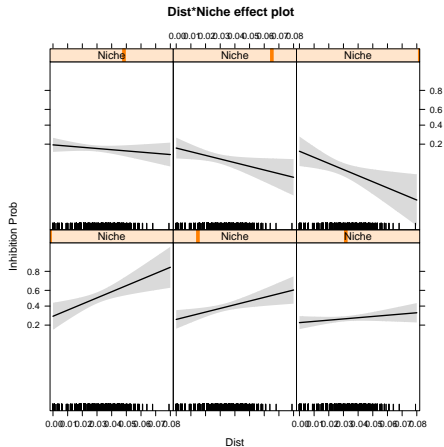


Figure : Interaction plot of Dist:Niche at PanFS

- Inhibition size: none of the predictors are significant

Allopatric Analysis: PanSC

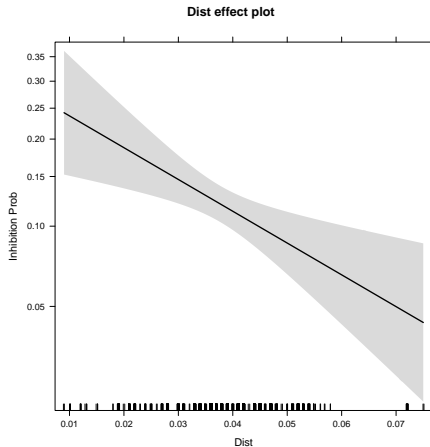


Figure : Effect plot of Dist at PanSC

- Inhibition size: Niche overlap is significant ($p \approx 0$). As Niche increases by 0.1 unit, inhibition size decreases 11.7%.

Allopatric Analysis: PanVB

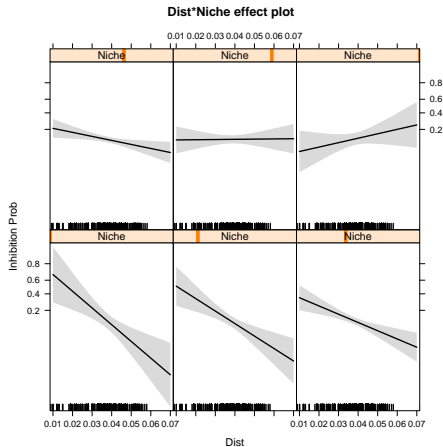


Figure : Interaction plot of Dist:Niche at PanVB

- Inhibition size: none of the predictors are significant.

Take home message

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- Be careful with the “prior” information provided by clients

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- How to interpret the results?
- Be careful with the “prior” information provided by clients
- e.g., pre-processed data, preliminary analysis

Thank you

Questions?