On the simple and partial Mantel tests with spatial data

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The (simple) Mantel test

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- **Goal:** "identifying subtle time-space clustering of disease, as may be occurring in leukemia"
- **Data:** \((x_i, y_i)_{i=1,...,n}\) observations of a space-time point process
- **Idea:**
  - transform data so as to get two univariate variables
  - compute correlation of transformed data
  - assess significance of correlation by some permutation method
The simple Mantel test: detailed algorithm

\[ D_x = \left| x_i - x_j \right|, \quad i, j \]

\[ D_y = \left| y_i - y_j \right|, \quad i, j \]

Compute the empirical correlation \( r \) between \( D_x \) and \( D_y \)

For \( \text{iter} = 1, N \)

1. Draw a random permutation \( \tau \) of \( 1, \ldots, n \)
2. Compute \( D_x^\tau = \left| x_{\tau(i)} - x_{\tau(j)} \right| \)
3. Compute the empirical correlation \( r^\tau \) between \( D_x^\tau \) and \( D_y \)

If |\( r \)| larger than some quantile estimated from the \( r^\tau \) values:

Report that there is "subtle time-space clustering of disease"
The simple Mantel test: detailed algorithm

- Compute $D^x = (|x_i - x_j|)_{i,j}$ and $D^y = (|y_i - y_j|)_{i,j}$
- Compute the empirical correlation $r$ between $D^x$ and $D^y$
- For $\text{iter } = 1, N$
  - Draw a random permutation $\tau$ of $1, \ldots, n$
  - Compute $D^x_\tau = (|x_{\tau(i)} - x_{\tau(j)}|)_{i,j}$
  - Compute the empirical correlation $r_\tau$ between $D^x_\tau$ and $D^y$
- If $|r|$ larger than some quantile estimated from the $r_\tau$ values:
  report that there is “subtle time-space clustering of disease”
The partial Mantel test


\[ x_i \text{ and } y_i \text{ observations of } p \text{ and } q \text{ variables for } n \text{ statistical units.} \]

Still attempts to assess the dependence between \( x \) and \( y \) need to "filter out" or "control for" the effect of a third variable \( z \) (e.g. \( z_i \) spatial coordinates of obs. \( i \)).
The partial Mantel test

The partial Mantel test


- $x_i$ and $y_i$: observations of $p$ and $q$ variables for $n$ statistical units.
- still attempts to assess the dependence between $x$ and $y$
- need to “filter out” or “control for” the effect of a third variable $z$ (e.g. $z_i$: spatial coordinates of obs. $i$)
The partial Mantel test: detailed algorithm

Compute $D_x = (|x_i - x_j|)_{i,j}$, $D_y = (|y_i - y_j|)_{i,j}$, and $D_z = (|z_i - z_j|)_{i,j}$.

Compute residuals $\tilde{D}_x$ of linear regressions $D_x \sim D_z$.

Compute residuals $\tilde{D}_y$ of linear regressions $D_y \sim D_z$.

Compute the empirical correlation $r$ between $\tilde{D}_x$ and $\tilde{D}_y$.

For $\text{iter} = 1, N$

1. draw a random permutation $\tau$ of $1, \ldots, n$.
2. compute $\tilde{D}_x^\tau$ as above for permuted $x_i$ values.
3. compute the empirical correlation $r^\tau$ between $\tilde{D}_x^\tau$ and $\tilde{D}_y$.

 Assess significance of $r$ by comparing to quantiles of $r^\tau$. 

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The partial Mantel test: detailed algorithm

- Compute $D^x = (|x_i - x_j|)_{i,j}$, $D^y = (|y_i - y_j|)_{i,j}$ and $D^z = (|z_i - z_j|)_{i,j}$
- Compute residuals $\tilde{D}^x$ of linear regressions $D^x \sim D^z$
- Compute residuals $\tilde{D}^y$ of linear regressions $D^y \sim D^z$
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- For iter = 1, N
  - draw a random permutation $\tau$ of 1, ..., $n$
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Mantel put into orbit

Mantel (Cancer Res., 1967) and Sokal (Sys. Zool., 1979) claimed that the approach was general and could be used to assess dependence between matrices of “distance.”

Features of the method:
- deals with multivariate data
- synthetizes data into a single numerical value
- does not seem to rely on any distributional assumption
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Posterity of Mantel’s work

Simple Mantel test [Mantel, 1967]:
\[ \geq 5000 \text{ ISI citations} \]

Partial Mantel test [Smouse et al., 1986]:
\[ \geq 1000 \text{ ISI citations} \]

Implemented in most ecology computer programs

Countless number of articles using the Mantel tests citing other supporting references

Routinely used in landscape genetics:
- genotypes,
- environmental variables,
- geographical coordinates

Practice strongly rooted:
Pr. XXX, Assoc. Editor J. of XXX:
"Referee 3 pointed out some issues with the Mantel tests but they are so widely used in landscape genetics that this comment can be disregarded."

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Is the Mantel test a statistical test?

What is a statistical test in Biology?

A method that returns a numerical value between 0 and 1. The lower the better.

More formal definition involves...

A null hypothesis

A method to derive a p-value

Some additional distributional assumptions
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Are the Mantel tests appropriate?

A common implementation:

$x_i$ multivariate genotype or phenotype. Due to population history and limited mixing in space $x$ is spatially-autocorrelated

$y_i$ multivariate descriptor of landscape (elevation, temperature, vegetation cover). Due to bio/geo-physical laws $y$ is spatially-autocorrelated

Interest in testing $H_0$: $x$ and $y$ are independent
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- Interest in testing $H_0$: $x$ and $y$ are independent.
A simulation study

Simulation to mimic the situation of one phenotypic variable and one environmental variable.

\[ s_1, ..., s_n \]

with \( n = 50 \) sites in \( [0, 1] \),

\[ x(s_1), ..., x(s_n) \]

values of a GRF with exponential covariance and

\[ y(s_1), ..., y(s_n) \]

values of a GRF with exponential covariance,

\[
\text{x and y independent commonly scale param. } \kappa_g
\]

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A simulation study

Simulation to mimic the situation of one phenotypic variable and one environmental variable.

- \( s_1, \ldots, s_n \) n=50 sites in \([0, 1]^2\)
- \( x(s_1), \ldots, x(s_n) \) values of a GRF with expo. covariance
- \( y(s_1), \ldots, y(s_n) \) values of a GRF with expo. covariance
- \( x \) and \( y \) independent
- common scale param. \( \kappa \)
Example of simulated data

Variable x

Variable y

Site-wise values

Pair-wise differences

Autocovariance and variogram functions

Cor(x,y) = 0.2

Cor(Dx,Dy) = -0.063

Correlation

Geographical (Euclidian) distance [m]
Simulation study (cont’)

- simulation above repeated for 200 realizations of $x$ and $y$
- p-values for simple Mantel test
- p-value for partial Mantel test with matrix $D^s$ entered to ”control the effect of space”.
- common scale param. $\kappa$ varying from 0 to 0.7
- plot of ordered p-values against quantiles of a uniform distribution
- Under $H_0$, the p-values should be uniformly distributed [Schweder and Spjøtvoll, 1982]
Qq-plots of p-values obtained on simulated data
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Figure: Left: simple Mantel test. Middle: partial Mantel test, no drift. Right: partial Mantel test, RFs with linear trend.
What’s wrong with the Mantel tests?

Mantel tests are based on permutation of one of the data vector entries. Permutation of $x$ values breaks the potential dependence between $x$ and $y$. Also breaks the spatial structure of $x$!!

The Mantel test fallacy: $\text{cor}(D_x \tau, D_y) \neq \text{cor}(D_x, D_y)$
What’s wrong with the Mantel tests?

Mantel tests are based on permutation of one of the data vector entries

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The Mantel test fallacy:

$$\text{cor}(D^x_{\tau}, D^y) \overset{\mathcal{L}}{\neq} \text{cor}(D^x, D^y)$$
Alternative approaches

- Testing independence between two point processes 
  - [Schlather et al., 2004]
- Modified t-test to account for auto-correlation 
  - [Clifford et al., 1989, Richardson and Clifford, 1991, Dutilleul et al., 1993]
- Extension to categorical data 
  - [Cerioli, 2002]
- Restricted permutations:
  - for clumped geostatistical data: within-population permutation
  - lattice data: shift permutation
- Testing in a GLMM framework
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Conclusion

Mantel tests are flawed in presence of structure in the data. This conclusion extends to other forms of structure (phylogenetic trees). A clear warning is timely.

Further work is needed on the side of computer program development. For more details, refer to the research report:


Thank you!
Conclusion

- Mantel tests are flawed in presence of structure in the data
- Conclusion extends to other form of structure (phylogentic trees)

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Research report:
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Research report:

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