Controlling the false positive rate of Granger causality tests in fMRI data

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Centre for Complex Systems and Brain and Mind Centre collaboration
USYD

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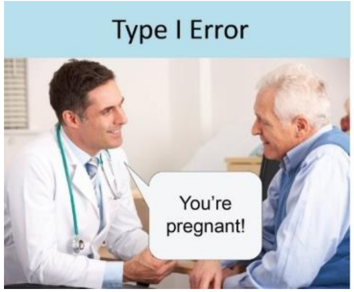
You’re pregnant!
Type II Error
You’re not pregnant!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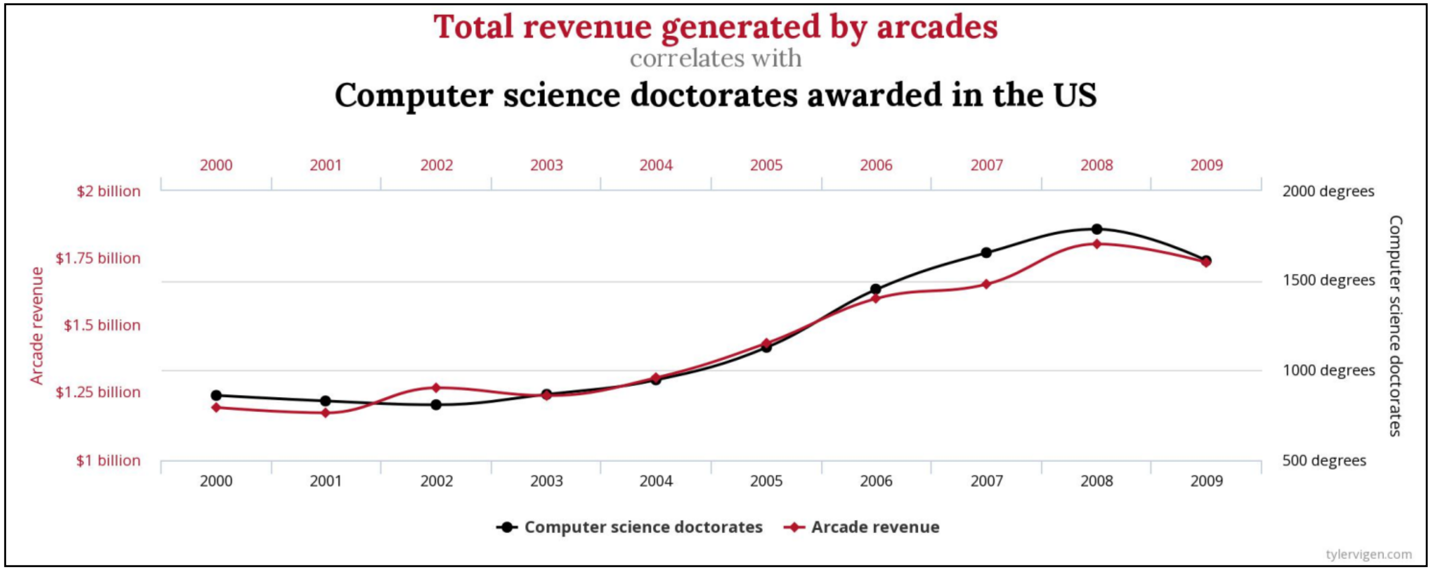
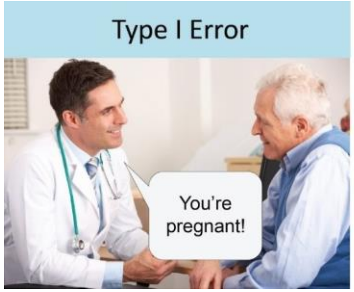

Total revenue generated by arcades
correlates with
Computer science doctorates awarded in the US
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
$2 billion
$1.75 billion
$1.5 billion
$1.25 billion
$1 billion
Arcade revenue
2000 degrees
1500 degrees
1000 degrees
500 degrees
Computer science doctorates
Computer science doctorates
Arcade revenue
tylervigen.com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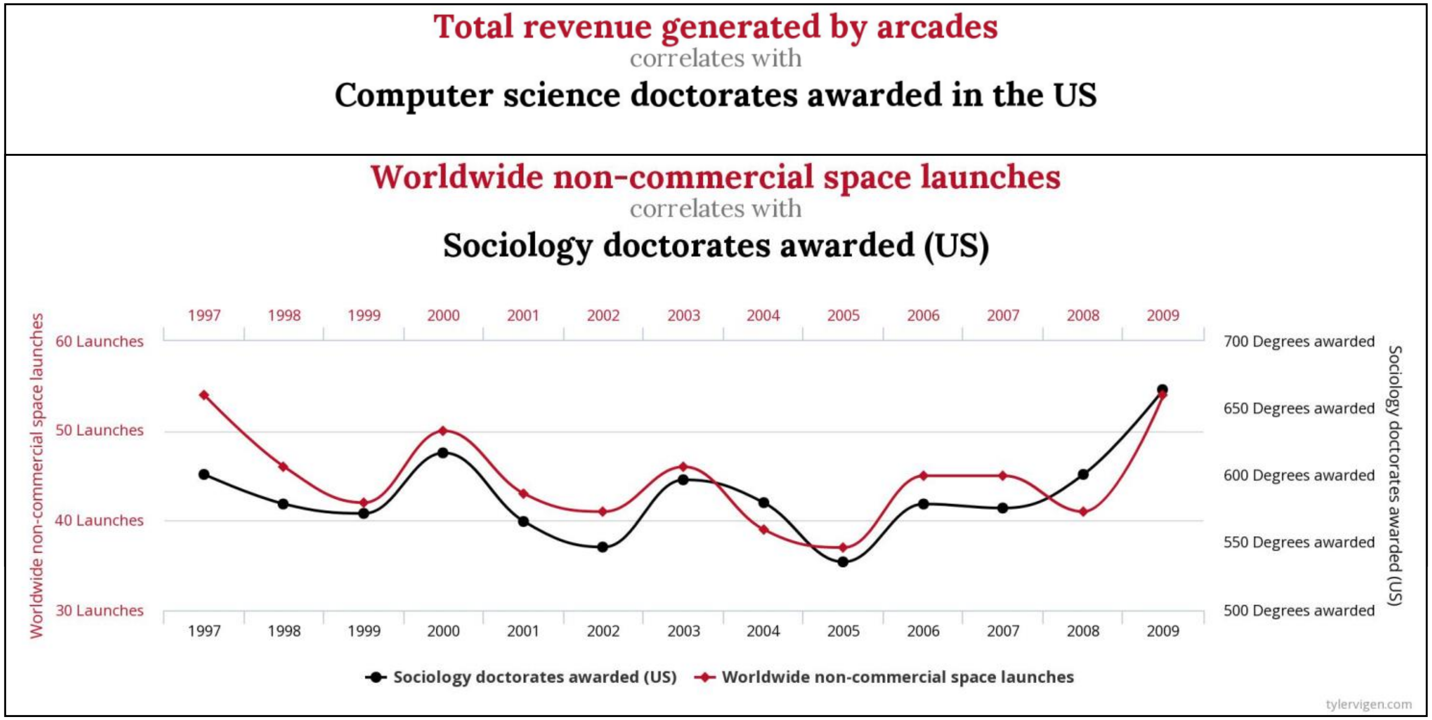
Total revenue generated by arcades
correlates with
Computer science doctorates awarded in the US
Worldwide non-commercial space launches
correlates with
Sociology doctorates awarded (US)
1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009
60 Launches
50 Launches
40 Launches
30 Launches
Worldwide non-commercial space launches
700 Degrees awarded
650 Degrees awarded
600 Degrees awarded
550 Degrees awarded
500 Degrees awarded
Sociology doctorates awarded (US)
Sociology doctorates awarded (US)
Worldwide non-commercial space launches
tylervigen.com

Total revenue generated by arcades
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correlates with
Sociology doctorates awarded (US)

Per capita consumption of mozzarella cheese
correlates with
Civil engineering doctorates awarded

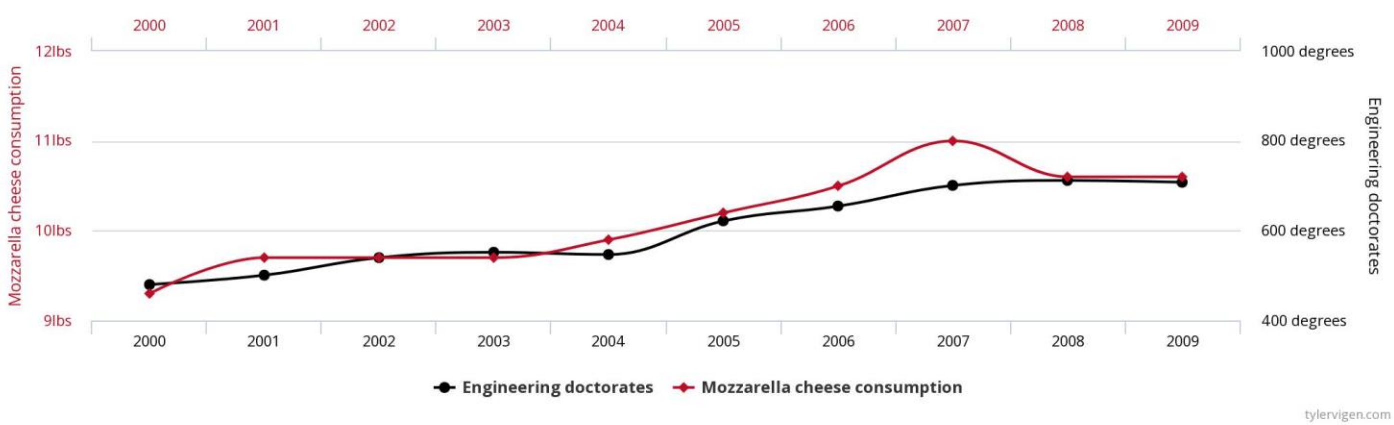
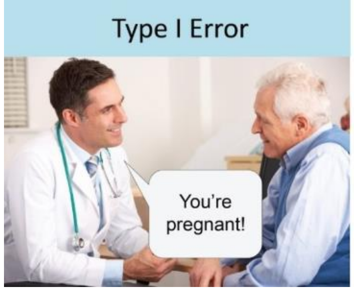


Image source: http://www.tylervigen.com/spurious-correlations

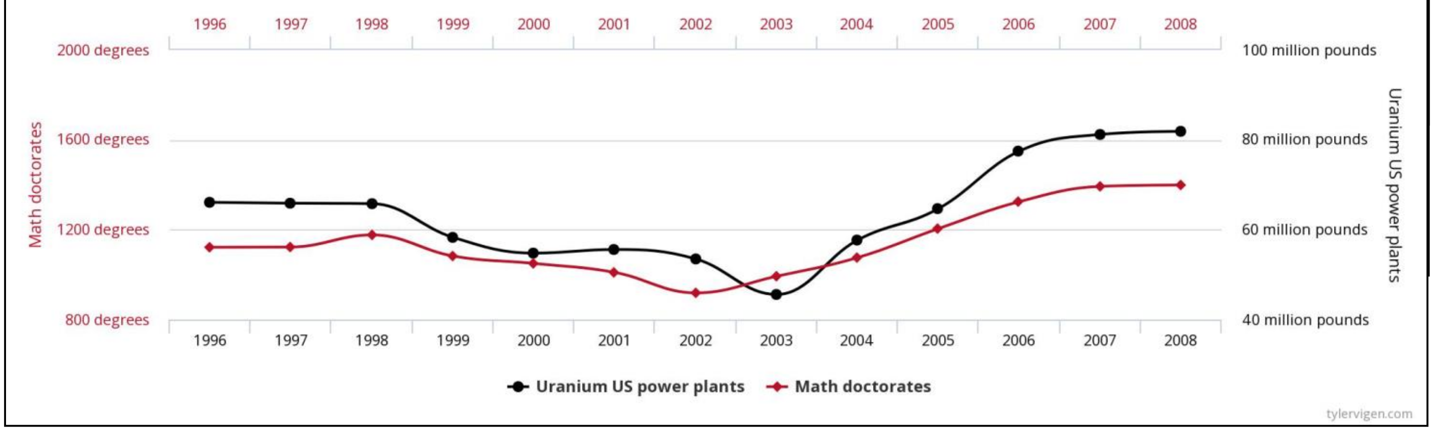


Total revenue generated by arcades
correlates with
Computer science doctorates awarded in the US

Worldwide non-commercial space launches
correlates with
Sociology doctorates awarded (US)

Per capita consumption of mozzarella cheese
correlates with
Civil engineering doctorates awarded

Math doctorates awarded
correlates with
Uranium stored at US nuclear power plants



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Main points

- These problems also occur in neuroscience
  - Naturally autocorrelated processes, e.g., fMRI and M/EEG
  - Autocorrelation through filtering (common to isolate 0.01 to 0.1 Hz for fMRI)

- A number of common dependence measures are overestimated:
  - Correlation
  - Granger causality
  - Mutual information
  - Conditional mutual information

- We propose methods for controlling this FPR

Increased false positive rates

Ridiculous question: Does one patient’s fMRI data influence another’s?

Increased false positive rates

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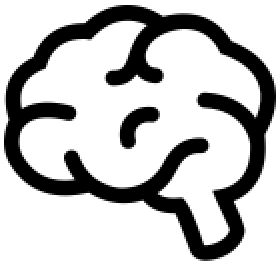

Increased false positive rates

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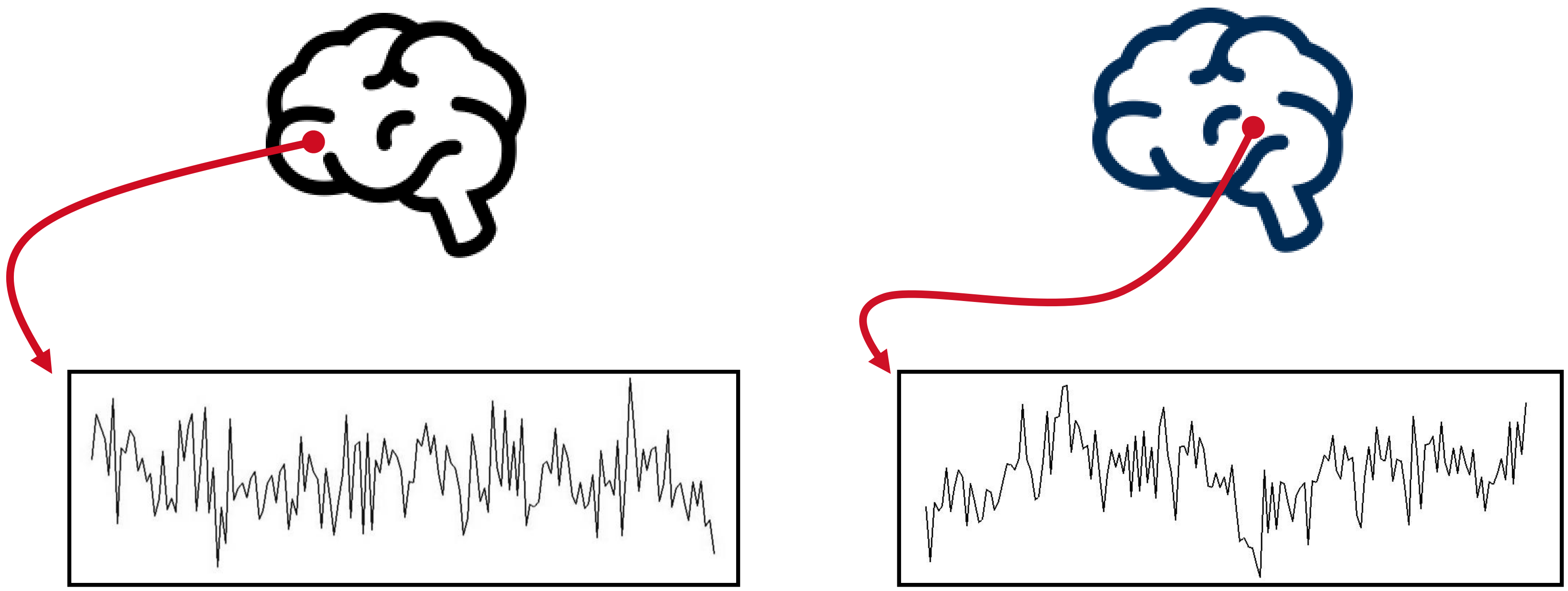

Increased false positive rates

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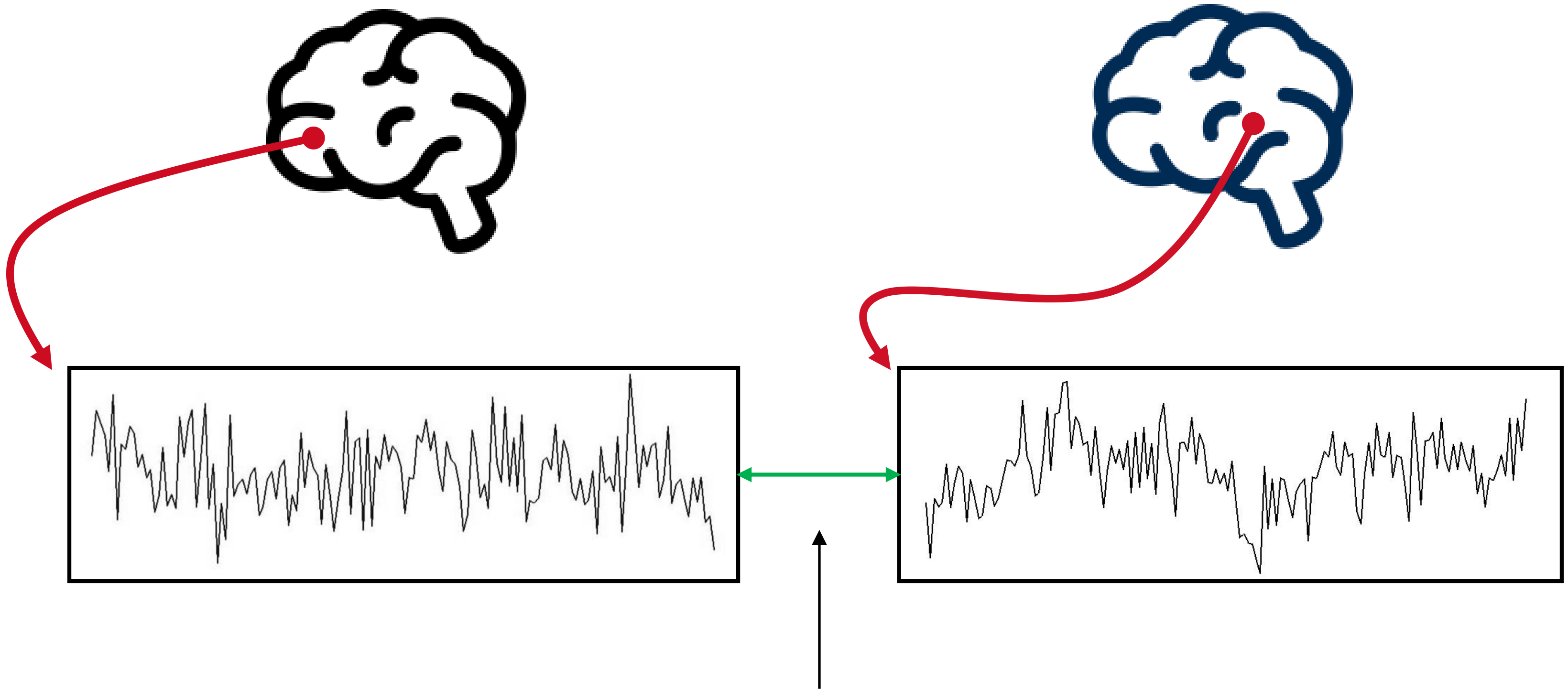
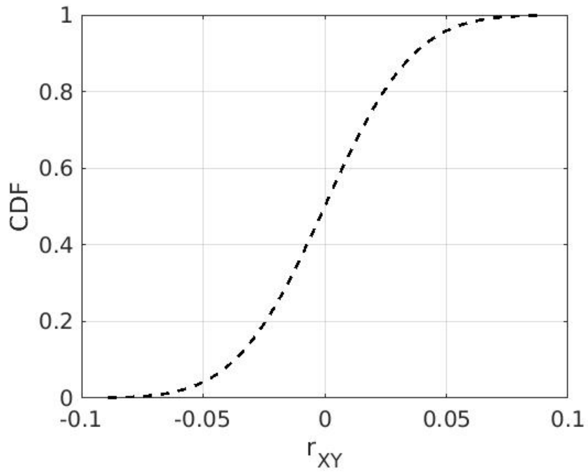


correlation, mutual information, Granger causality, etc.

Increased false positive rates

Test correlation against a t distribution…

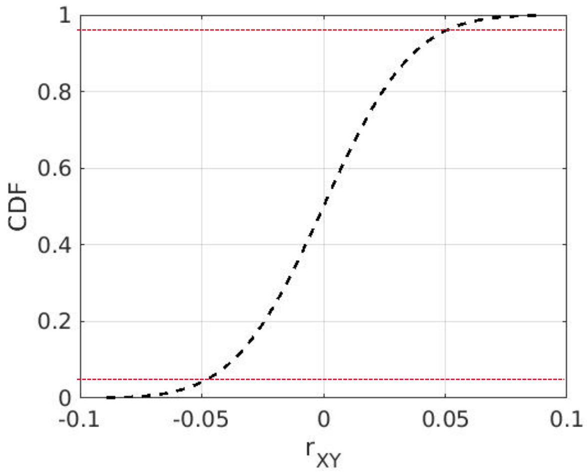
$$r_{XY} \sim t(N-2)$$



Increased false positive rates

…at a nominal p-value of 5%

$$r_{XY} \sim t(N-2)$$



Increased false positive rates

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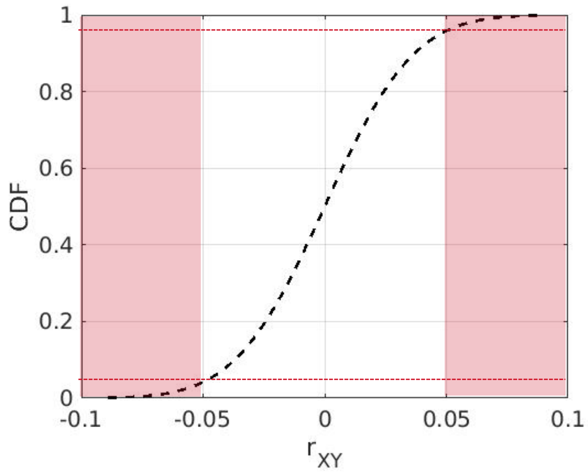
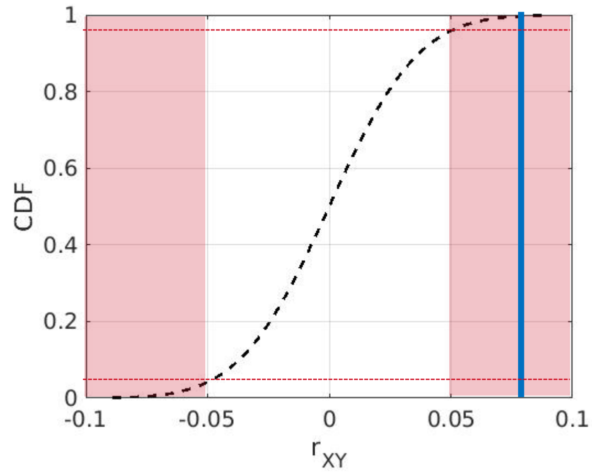


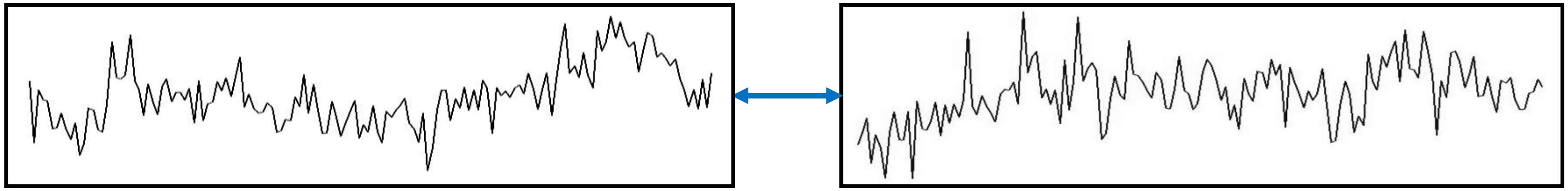
Increased false positive rates

Answer: 1/1 tests indicate true (100%)…

$$r_{XY} \sim t(N-2)$$



$- r_{X_1 Y_1}$

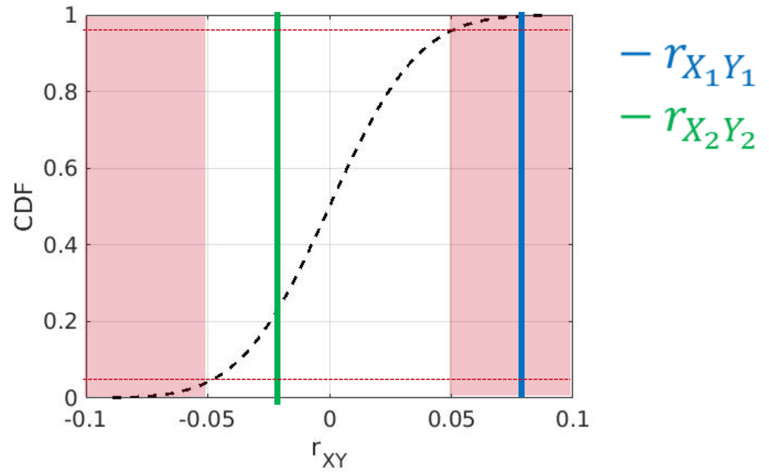


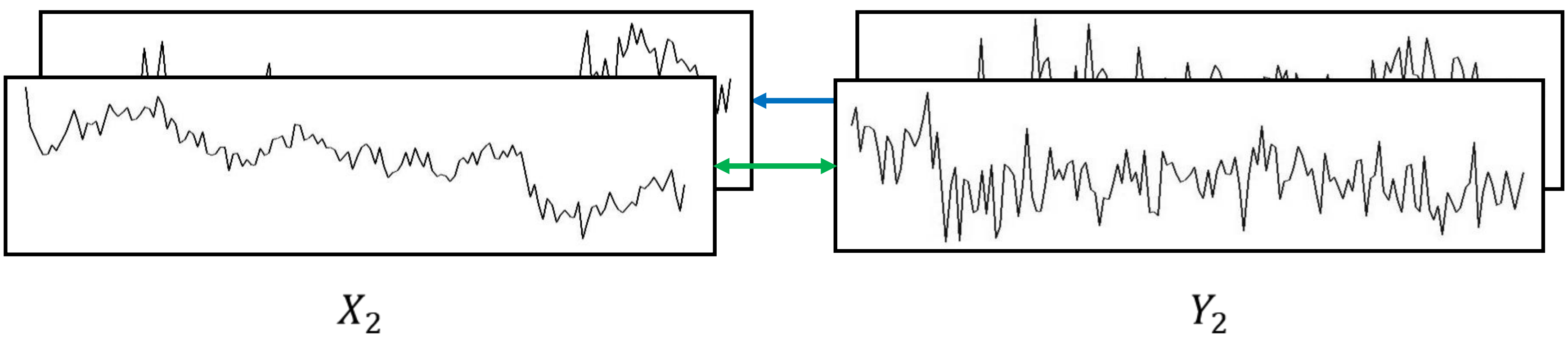
X_1 Y_1

Increased false positive rates

Answer: 1/2 tests indicate true (50%)…

$$r_{XY} \sim t(N-2)$$

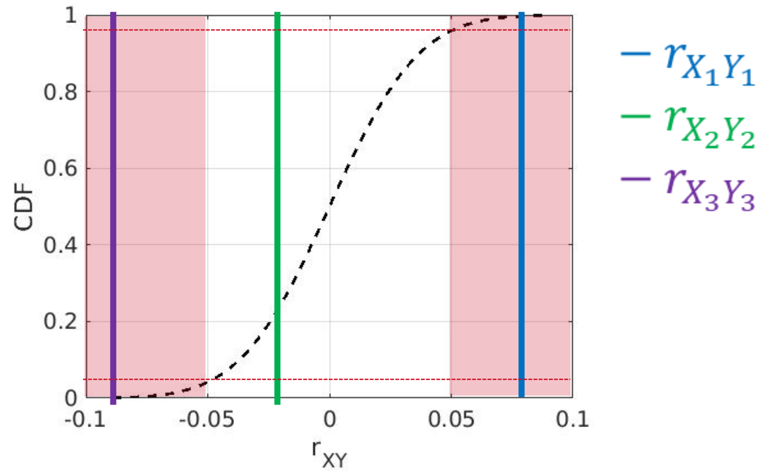


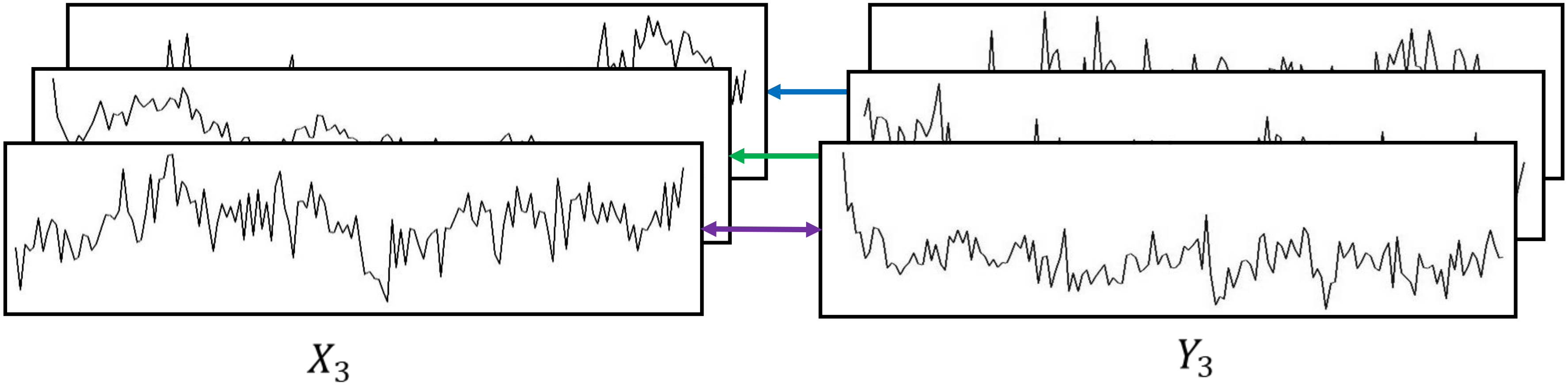


Increased false positive rates

Answer: 2/3 tests indicate true (67%)…

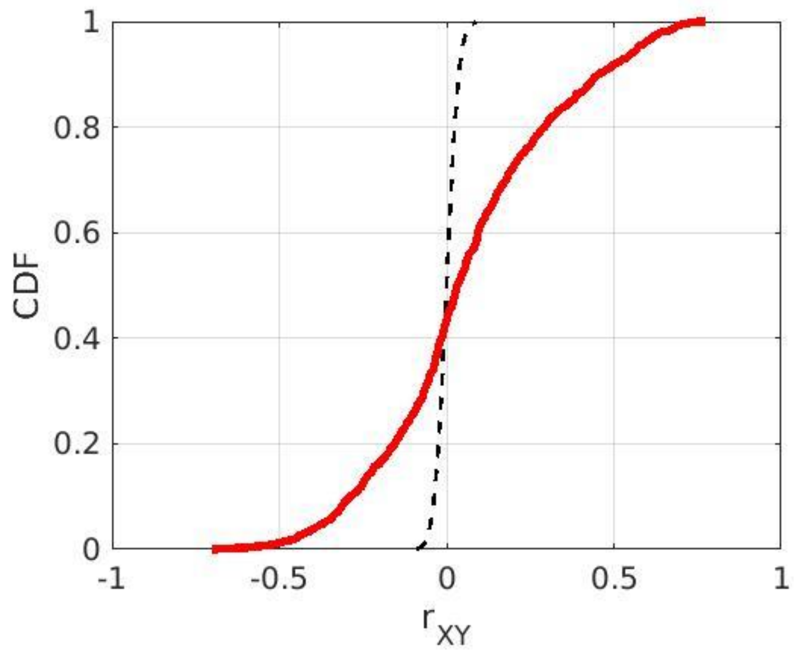
$$r_{XY} \sim t(N-2)$$





Increased false positive rates

Answer: 781/1000 tests indicate true (78%)



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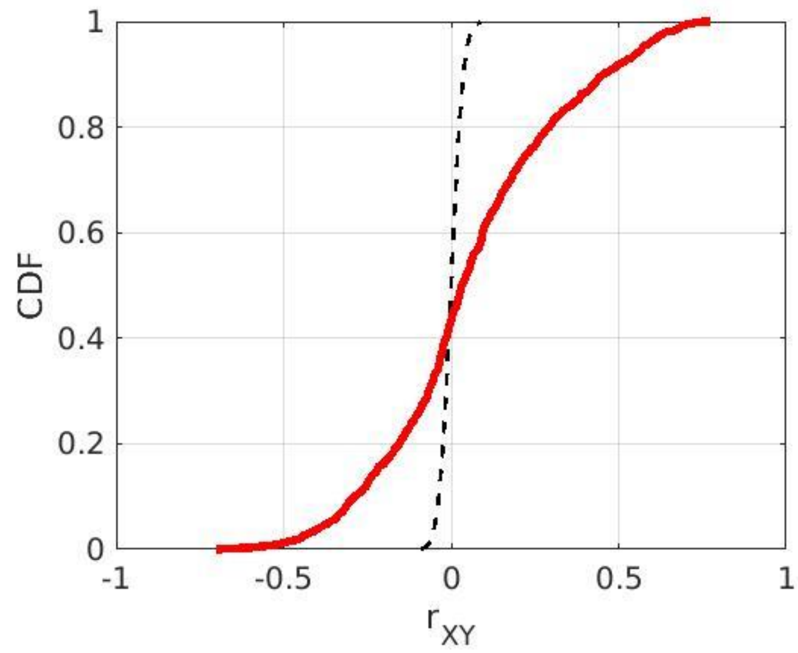

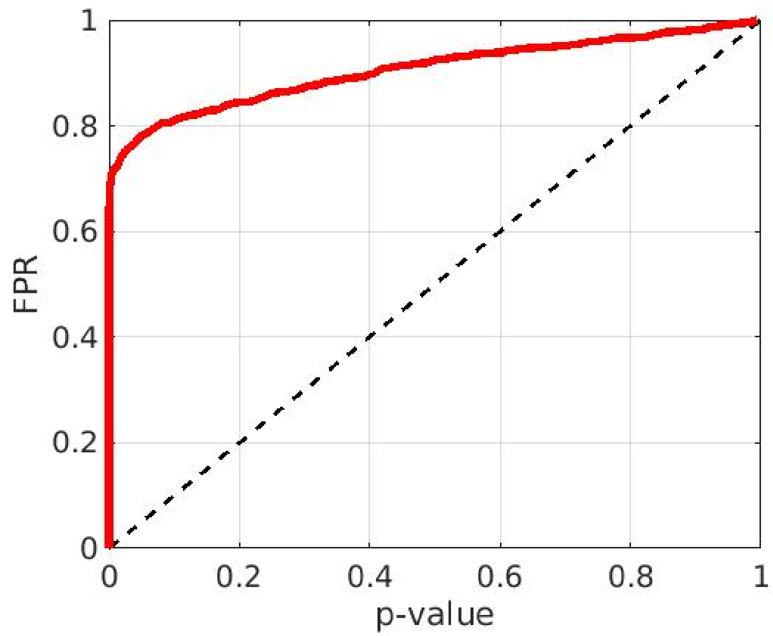

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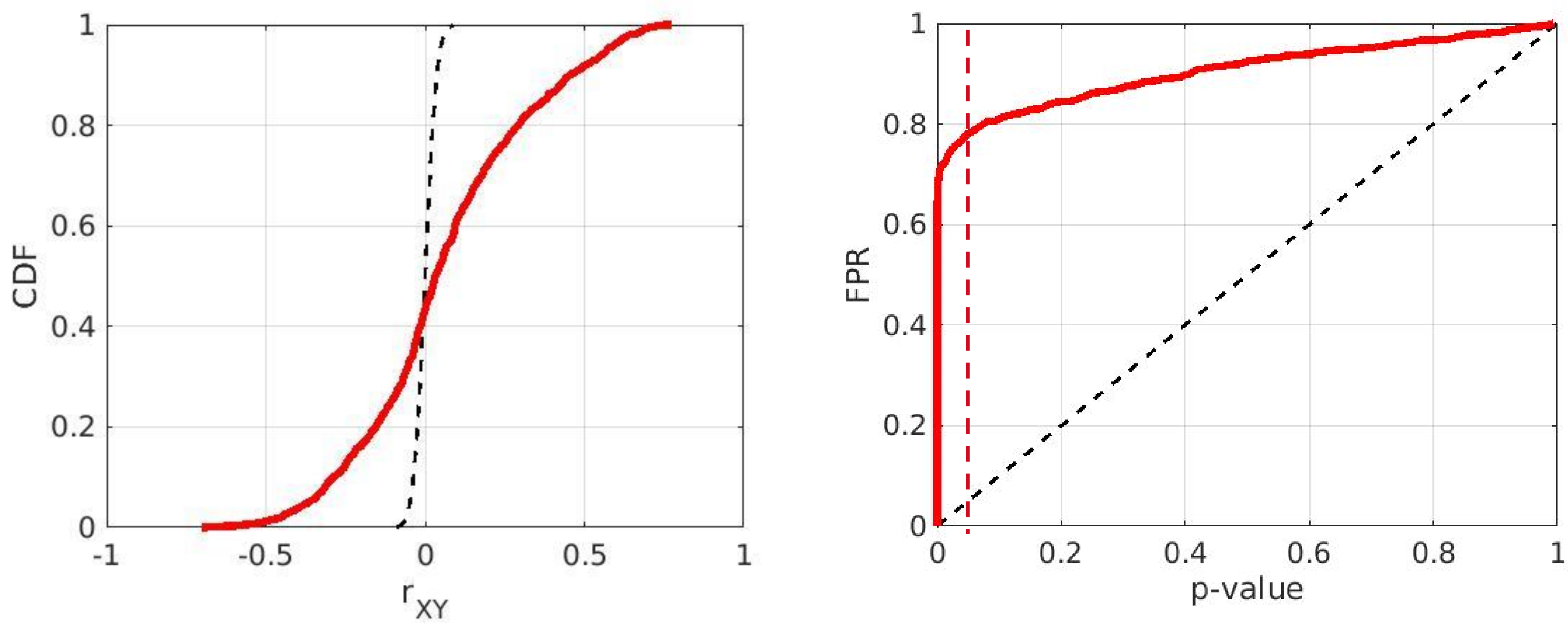


Increased false positive rates

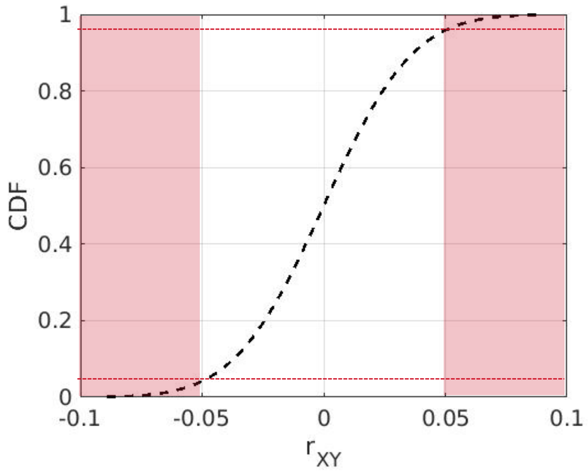
- Higher autocorrelation increases the FPR of sample correlation
  - This has been known since Yule/Pearson's work in the early 20th century

- How do we fix it?
  - **Bartlett's formula**
    - Correct the sample size based on autocorrelation of univariate signals
    - Does the process pass the t-test with effective sample size?
  - **Granger causality**
    - Define process through autocovariance
    - Does adding in another process improve predictability?

Bartlett's formula

› Testing Pearson correlation:

$$r_{XY} \sim t(N-2)$$



Bartlett's formula

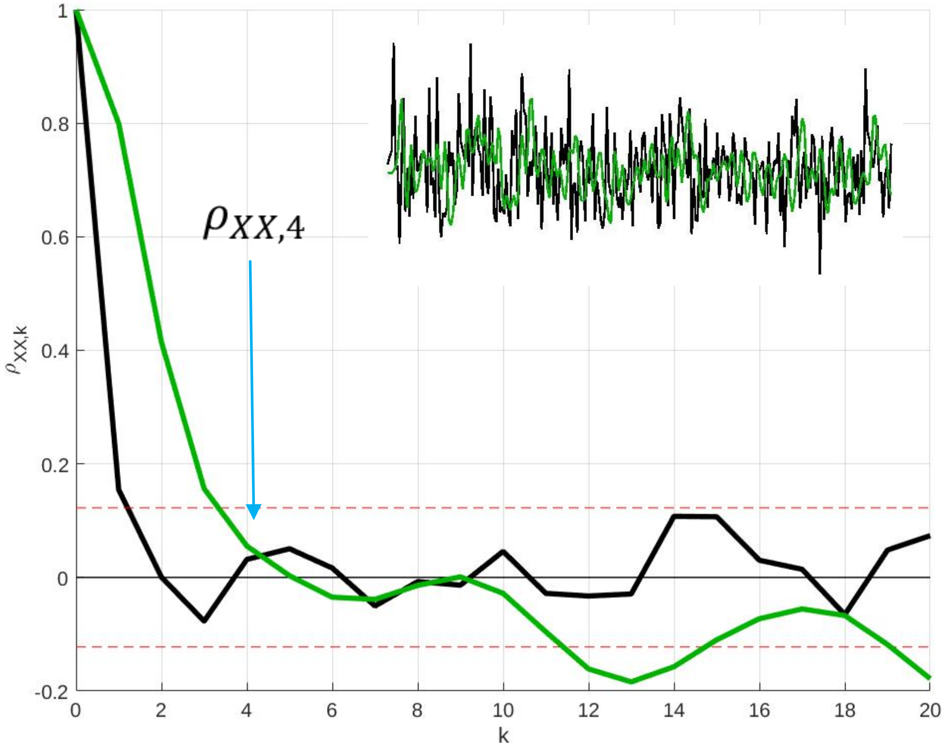
› Testing Pearson correlation:

$$r_{XY} \sim t(N-2)$$

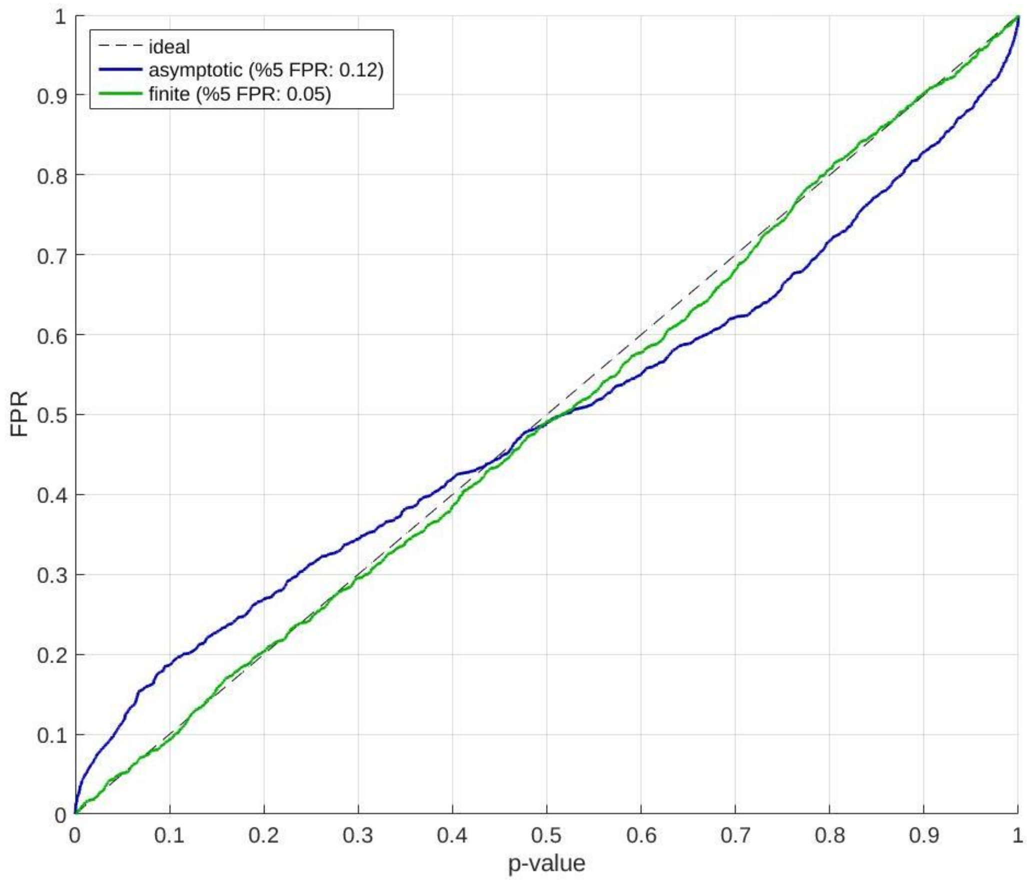
› Under autocorrelation:

$$r_{XY} \sim t(N_{eff}-2)$$

$$N_{eff} = \frac{N}{\sum_k \rho_{XX,k}\rho_{YY,k}}$$



Bartlett's formula

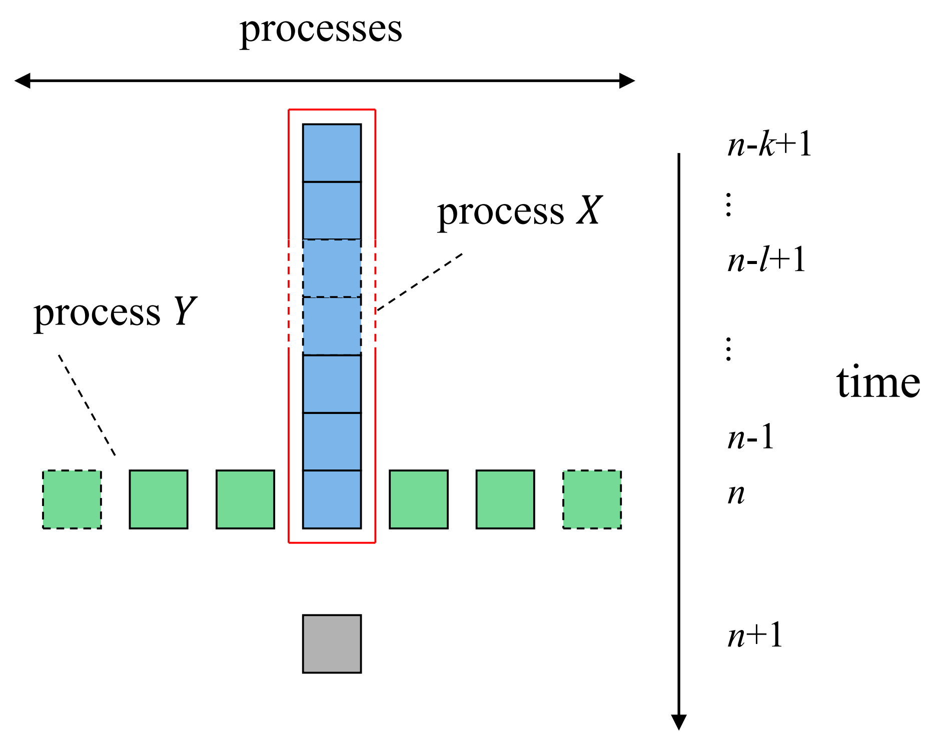


- Asymptotic distribution is **inefficient**
- Bartlett's formula corrects to nominal FPR

Granger causality

› Build a target AR process

$$X_{n+1} = a_1 X_n + \cdots + a_k X_{n-k+1} + \epsilon_{1n}$$



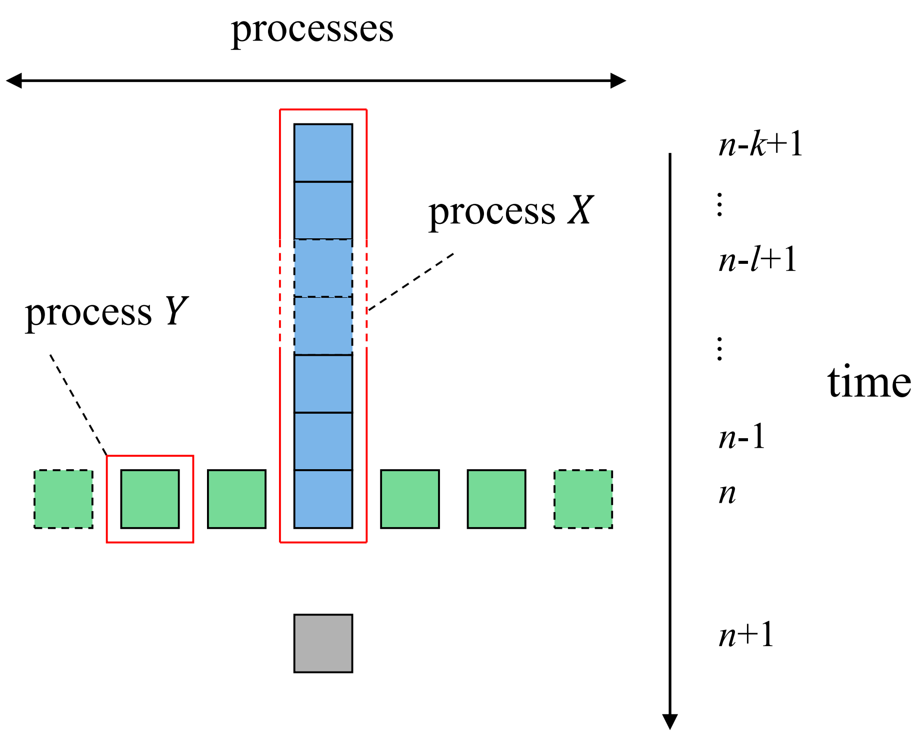
Granger causality

- Build a target AR process

$$X_{n+1} = a_1 X_n + \cdots + a_k X_{n-k+1} + \epsilon_{1n}$$

- Include another (source) process

$$X_{n+1} = a_1 X_n + \cdots + a_k X_{n-k+1} + \epsilon_{2n} \\ + b_1 Y_n + \cdots + b_l Y_{n-l+1}$$



Granger causality

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- Include another (source) process

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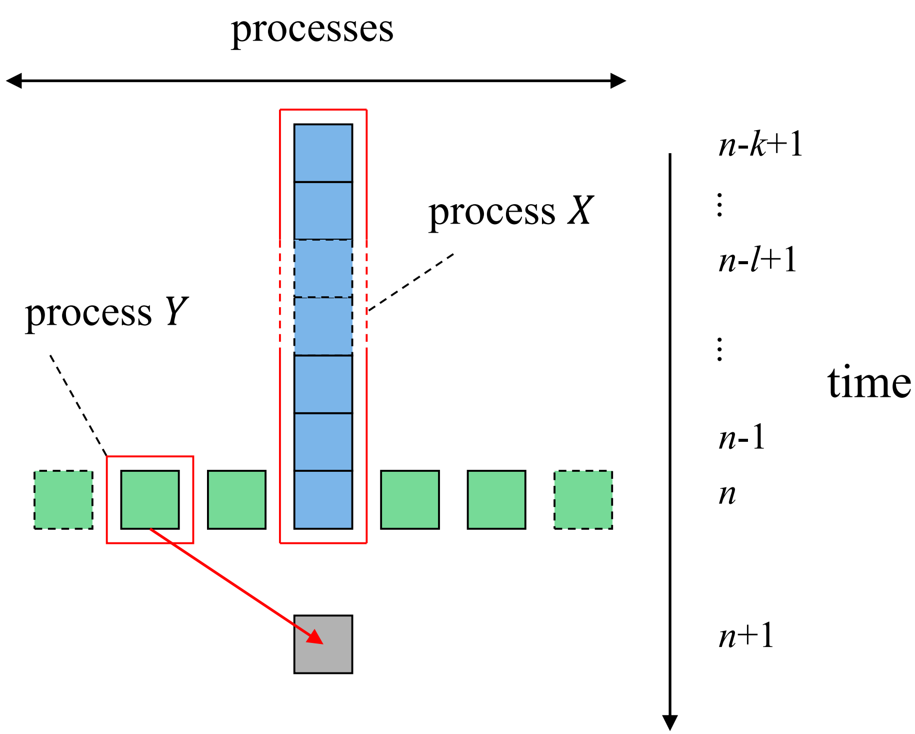
$$+ b_1 Y_n + \cdots + b_l Y_{n-l+1}$$

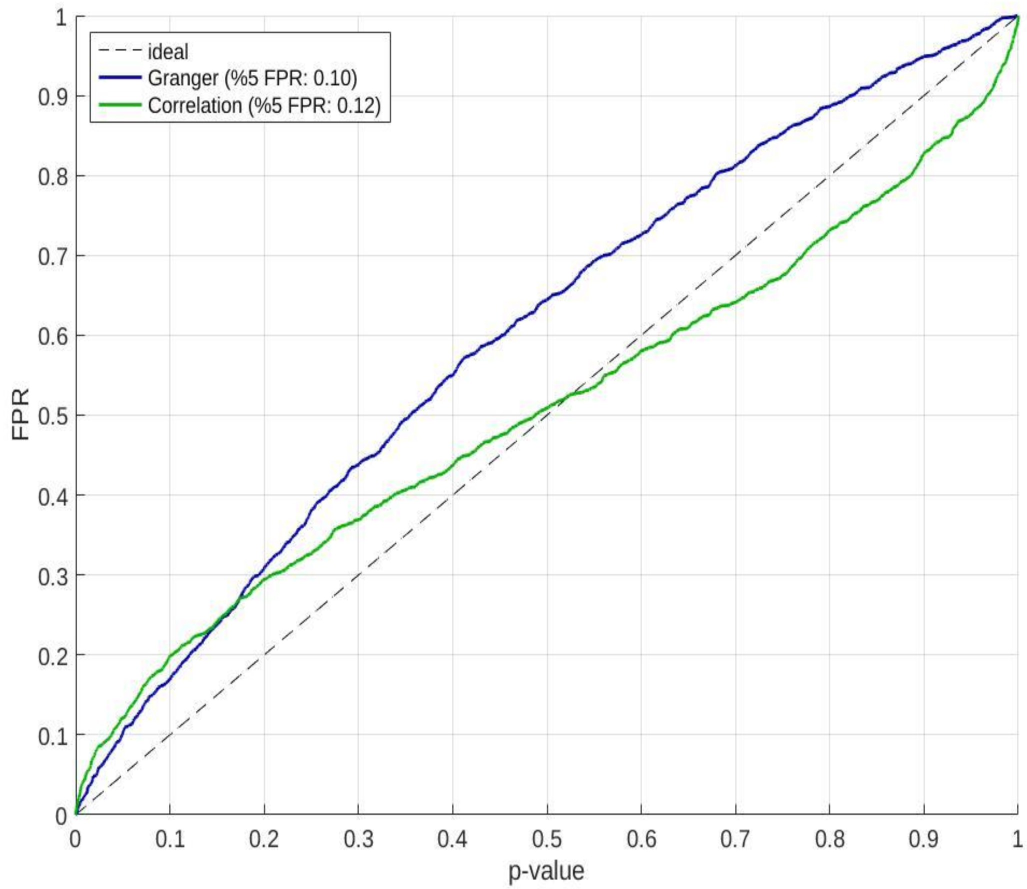
- Test using Wilk's theorem:

$$N\, G_{Y \to X}(k, l) \sim \chi^2(l)$$

$$G_{Y \to X}(k, l) = \ln\left(\frac{\sum \epsilon_{1n}^2}{\sum \epsilon_{2n}^2}\right)$$



Granger causality



- Asymptotic distribution is **biased**
- Slightly lower FPR than correlation

Bartlett's formula and Granger causality

- Bartlett's formula controls FPR for correlation with univariate processes
  - Multivariate generalization is known as canonical correlations
    - These are also inefficient under serial correlation

- Granger causality reduces but does not control FPR
  - Naturally extends to multiple time series
    - FPR increases for:
      - more dimensions, or
      - higher order AR/filtering

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Sampling distribution of Granger causality

› How do we control for the FPR of Granger?

- Granger causality is equivalent to **conditional mutual information** (Barnett et al., 2009)
- In our paper, we show CMI for a univariate source and target can be expressed as a squared **partial correlation**
- Bartlett’s formula can be used to obtain the sampling distributions
- Through chain rule, multivariate measures are sums of squared PC

Sampling distribution of partial correlation and CMI

- Granger causality is partial correlation squared

$$G_{Y \to X}(1,1) = -\ln\left(1 - r^2_{X_{n+1}Y_n \cdot X_n}\right)$$

Sampling distribution of partial correlation and CMI

› Granger causality is partial correlation squared

$$G_{Y\to X}(1,1) = -\ln\left(1 - r^2_{X_{n+1}Y_n\cdot X_n}\right)$$

› Partial correlation follows same distribution as correlation with less effective samples based on the number of conditionals

$$r_{X_{n+1}Y_n\cdot X_n} \sim t(N_{eff} - 3)$$

Sampling distribution of partial correlation and CMI

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$$r_{X_{n+1}Y_n\cdot X_n} \sim t(\underbrace{N_{eff}} - 3)$$

Bartlett's formula using residuals of $X_{n+1} \mid X_n$ and $Y_n \mid X_n$

Sampling distribution of partial correlation and CMI

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$$r_{X_{n+1}Y_n \cdot X_n} \sim t(N_{eff} - 3)$$

- Squaring t-distribution gives an F-distribution

$$r^2_{X_{n+1}Y_n \cdot X_n} \sim F(1, N_{eff} - 3)$$

Sampling distribution of partial correlation and CMI

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$$r_{X_{n+1}Y_n\cdot X_n} \sim t(N_{eff} - 3)$$

- Squaring t-distribution gives an F-distribution

$$r^2_{X_{n+1}Y_n\cdot X_n} \sim F(1, N_{eff} - 3)$$

- This is the approximate sampling distribution of Granger (exact can be Monte Carlo sampled inside log)

$$G_{Y\rightarrow X}(1,1) \sim F(1, N_{eff} - 3)$$

Multivariate Granger causality

› By chain rule, increasing the source dimension simply adds more terms

$$G_{Y\to X}(k,l) \approx r^2_{X_{n+1}Y_n\cdot X_n^{(k)}} + r^2_{X_{n+1}Y_{n-1}\cdot\{X_n^{(k)},Y_n\}} + \cdots + r^2_{X_{n+1}Y_{n-l+1}\cdot\{X_n^{(k)},Y_n,\ldots,Y_{n-l+2}\}}$$

Multivariate Granger causality

- By chain rule, increasing the source dimension simply adds more terms

$$G_{Y\to X}(k,l) \approx \underbrace{r^2_{X_{n+1}Y_n \cdot X_n^{(k)}}}_{F\left(1,\,N_{eff,1}-k-2\right)} + \underbrace{r^2_{X_{n+1}Y_{n-1}\cdot\{X_n^{(k)},Y_n\}}}_{F\left(1,\,N_{eff,2}-k-1-2\right)} + \cdots + \underbrace{r^2_{X_{n+1}Y_{n-l+1}\cdot\{X_n^{(k)},Y_n,\ldots,Y_{n-l+2}\}}}_{F\left(1,\,N_{eff,l}-k-l-2\right)}$$

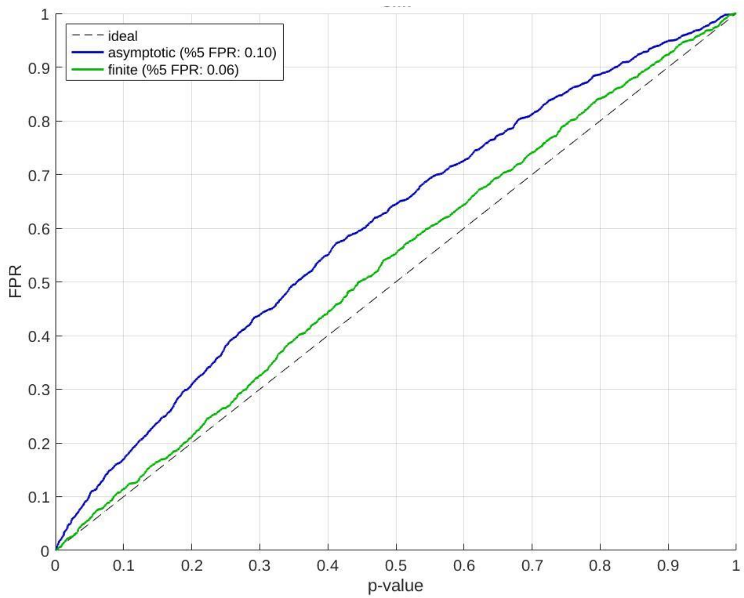
$$\cdots$$

- These terms have different DOFs, and we Monte Carlo sample the distribution

Numerical evaluation

Simulate with N=512, inducing autoregression through **FIR filter**

~8th Order AR
(8th Order FIR filter)



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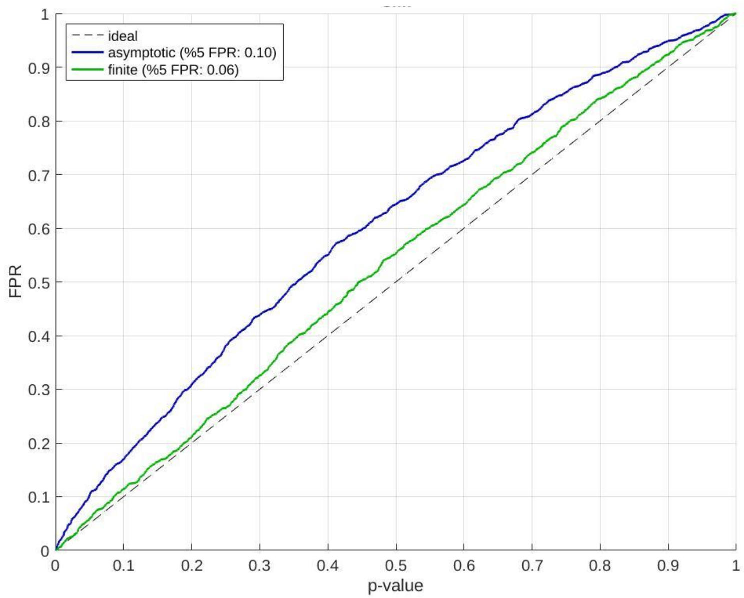
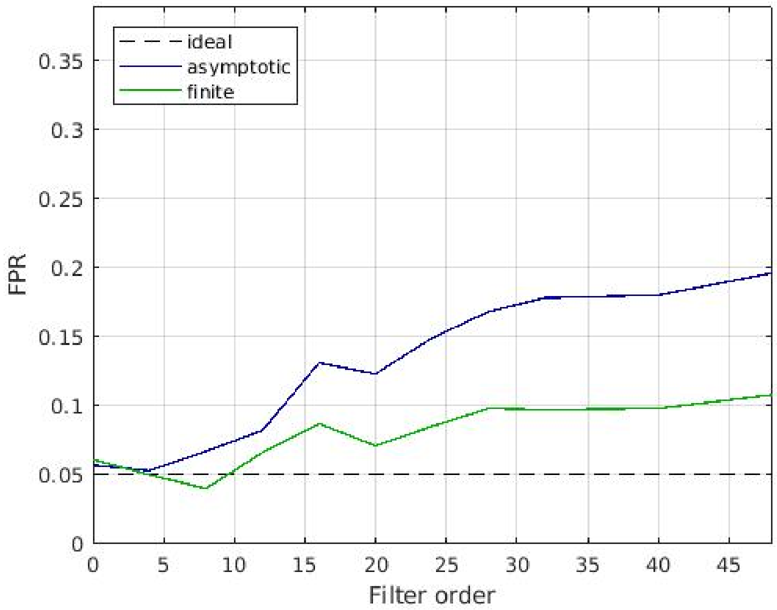


Increasing filter order



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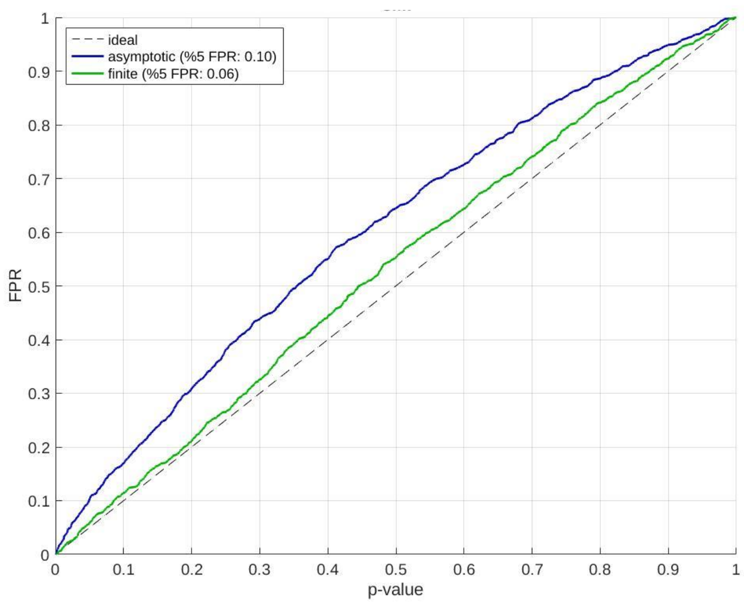
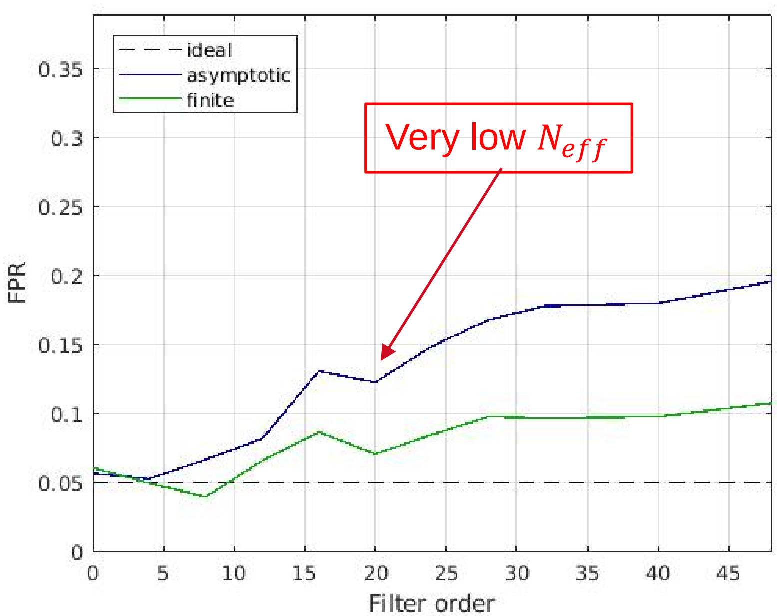


Increasing filter order



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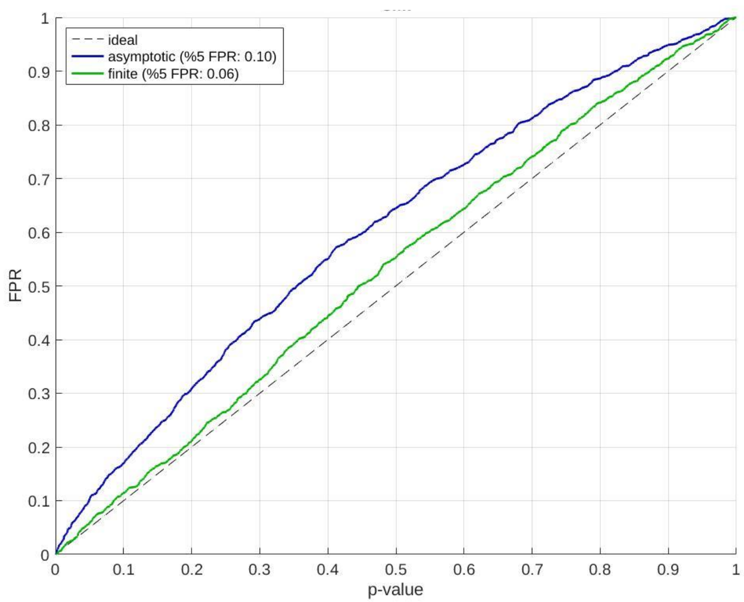
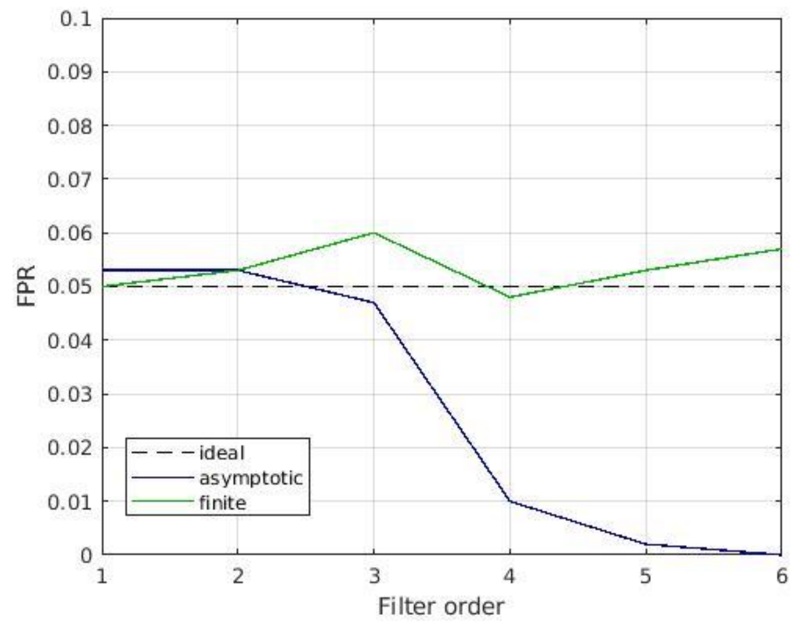


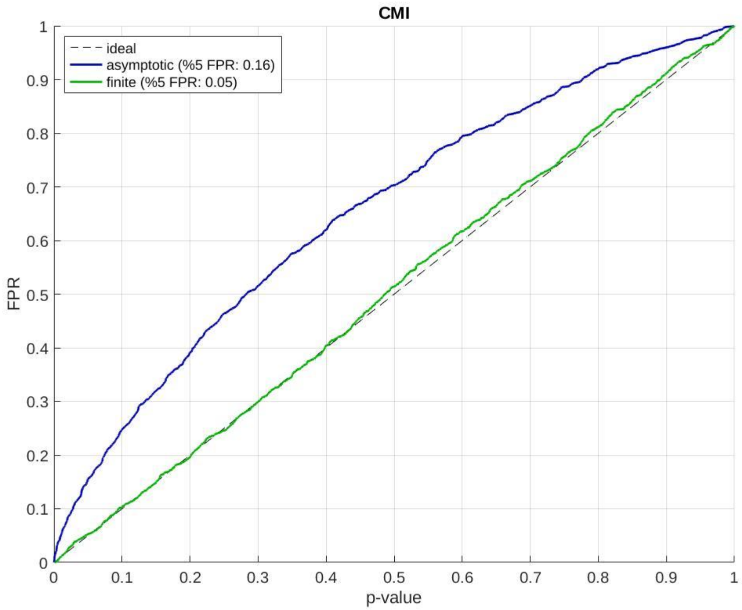
Increasing dimensionality



Numerical evaluation

Simulate with N=512, inducing autoregression through **IIR filter**

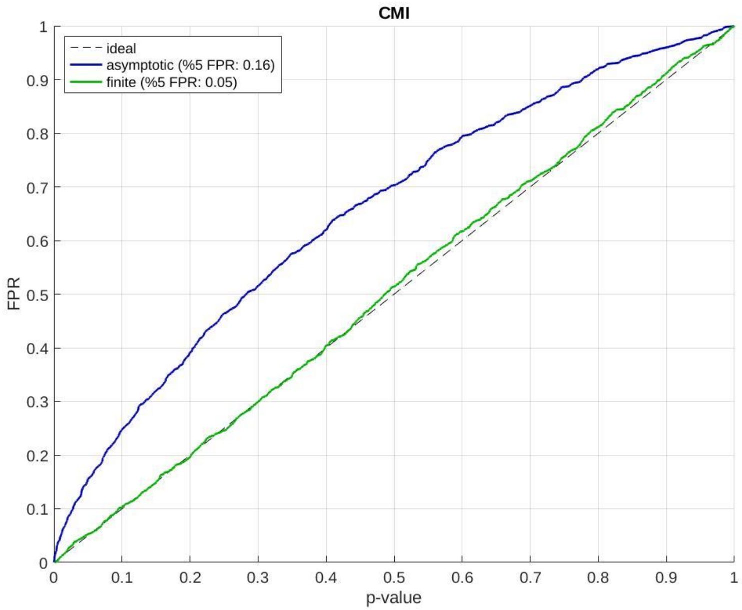
~16th Order AR
(4th Order IIR filter)



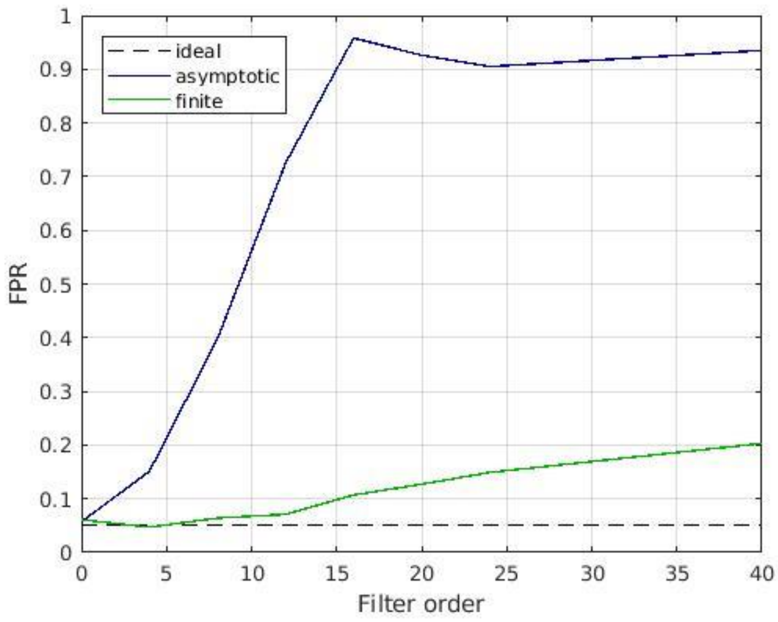
Numerical evaluation

Simulate with N=512, inducing autoregression through **IIR filter**

~16th Order AR
(4th Order IIR filter)



Increasing filter order



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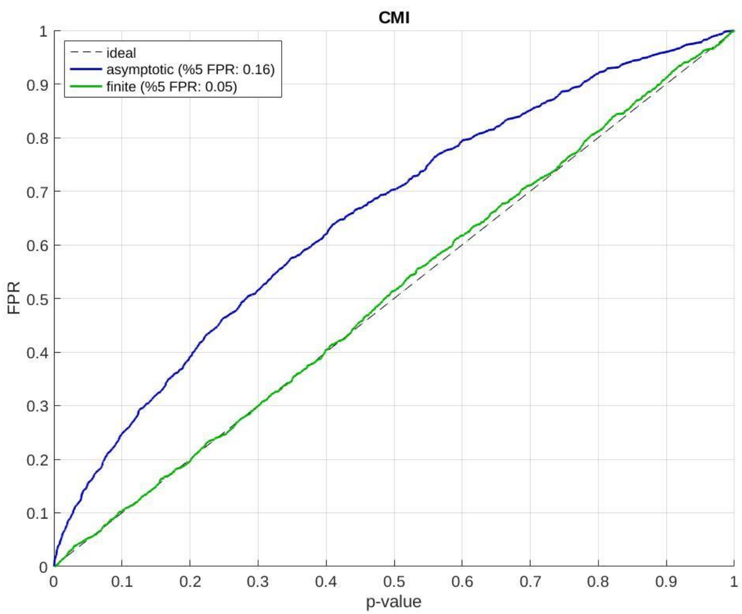
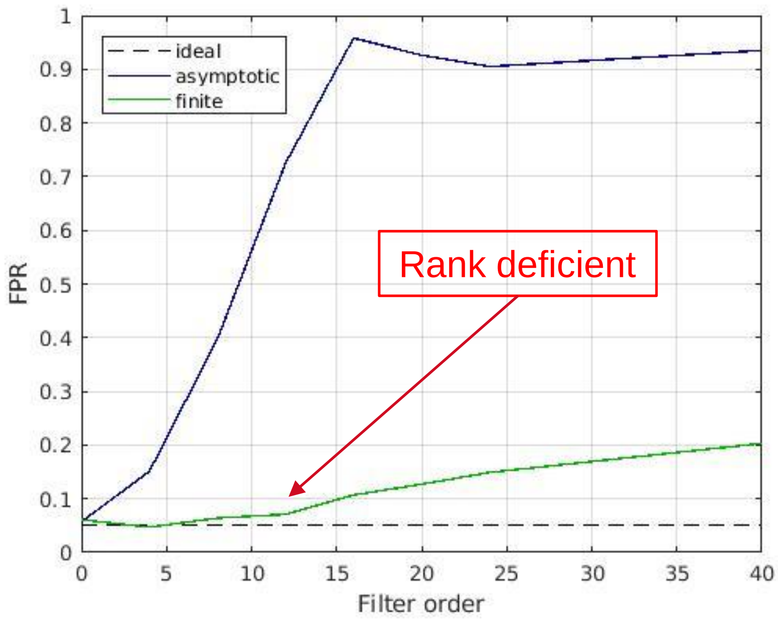


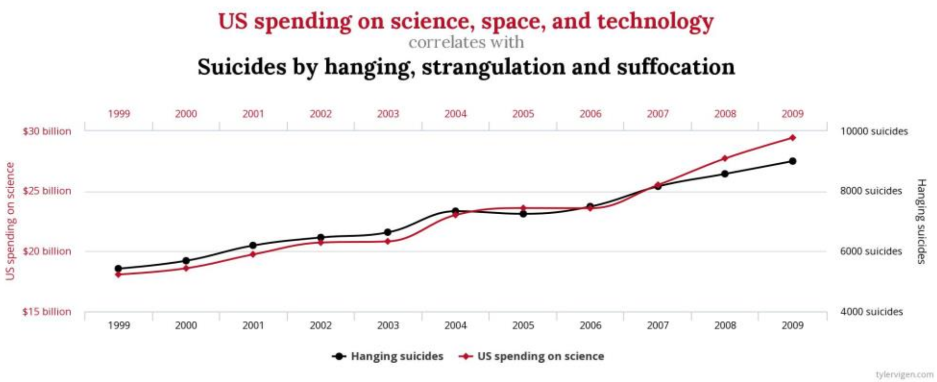
Increasing filter order



Take home messages

- Important dependence measures exhibit bias for autocorrelated Gaussian processes
- These measures can be represented as sums of squared partial correlations
- This representation allows us to derive the sampling distribution
- Before our work, these distributions were only valid asymptotically

Thank you!


US spending on science, space, and technology
correlates with
Suicides by hanging, strangulation and suffocation
$30 billion
$25 billion
$20 billion
$15 billion
US spending on science
10000 suicides
8000 suicides
6000 suicides
4000 suicides
Hanging suicides
1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009
Hanging suicides
US spending on science
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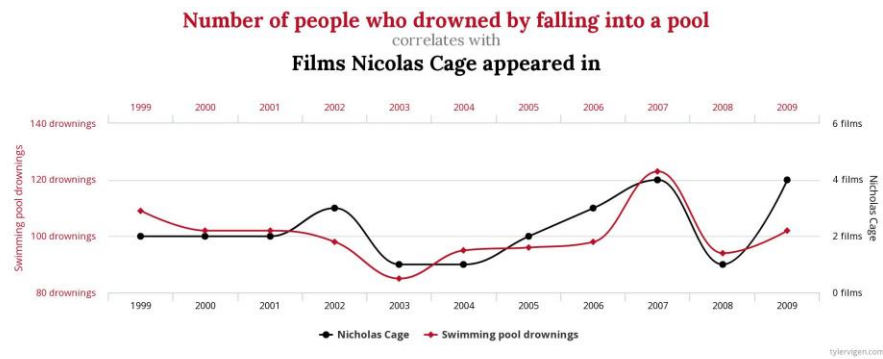
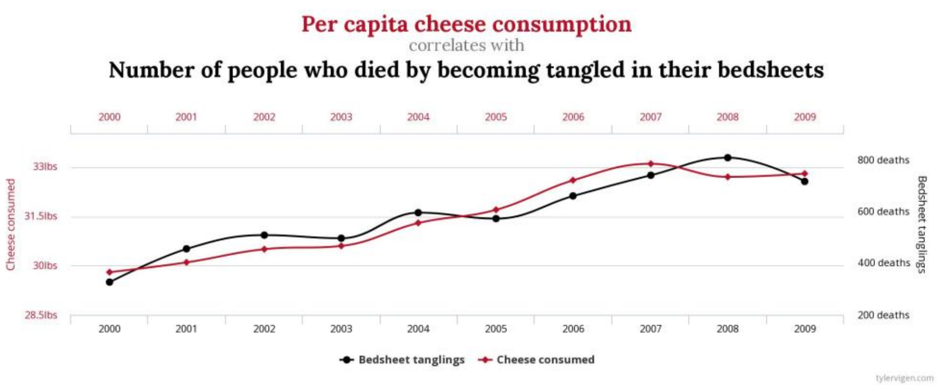
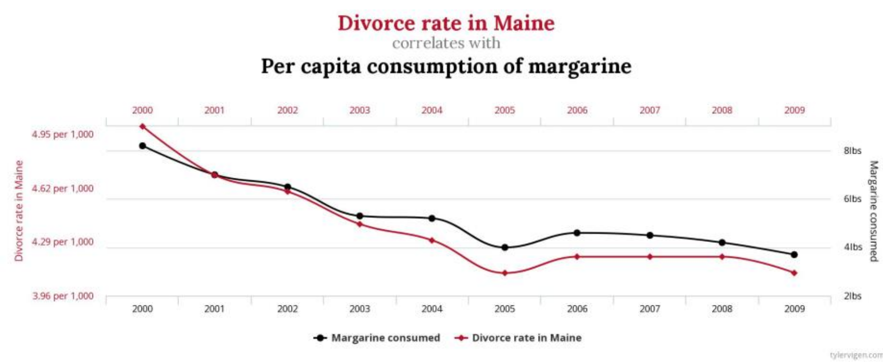

Number of people who drowned by falling into a pool
correlates with
Films Nicolas Cage appeared in
140 drownings
120 drownings
100 drownings
80 drownings
Swimming pool drownings
6 films
4 films
2 films
0 films
Nicolas Cage
1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009
Nicolas Cage
Swimming pool drownings
tylervigen.com


Per capita cheese consumption
correlates with
Number of people who died by becoming tangled in their bedsheets
33lbs
31.5lbs
30lbs
28.5lbs
Cheese consumed
800 deaths
600 deaths
400 deaths
200 deaths
Bedsheet tanglings
2000 2001 2002 2003 2004 2005 2006 2007 2008 2009
Bedsheet tanglings
Cheese consumed
tylervigen.com


Divorce rate in Maine
correlates with
Per capita consumption of margarine
4.95 per 1,000
4.62 per 1,000
4.29 per 1,000
3.96 per 1,000
Divorce rate in Maine
8lbs
6lbs
4lbs
2lbs
Margarine consumed
2000 2001 2002 2003 2004 2005 2006 2007 2008 2009
Margarine consumed
Divorce rate in Maine
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