



Mathematics and Statistics

$$\int_{M} d\omega = \int_{\partial M} \omega$$

Mathematics 4MB3/6MB3 Mathematical Biology

Instructor: David Earn

Lecture 3 Epidemic Data Monday 23 September 2019

- You should have received an invitation to do the contributions survey for Assignment 1. Please do it TODAY (e.g., during the mid-class break).
- Don't stress about the ratings about each other's contributions. The issue is whether some group members did not pull their weight. If somebody didn't try and others had to pick up the slack, that person should be penalized. I will not penalize somebody because they tried but felt they didn't contribute as much to the final document as they could have. Do try to even out the work across the assignments.
- Make sure everyone in your group gets a chance to be in control of the LATEX for one assignment.

More Announcements!

Assignment 2:

Due Monday 7 October 2019 by e-mail before class.

Midterm test:

- Date: Monday 4 November 2019
- Time: 11:30am–1:30pm
- Location: in class, ETB-237

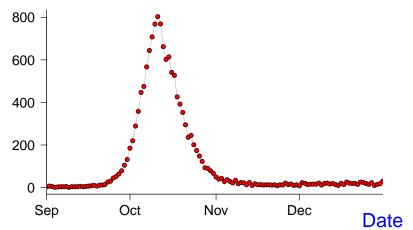


Who is here?

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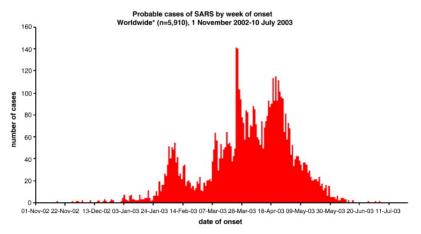
P&I Mortality, Philadelphia, 1918

P&I Deaths



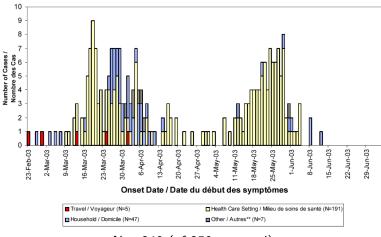
Motivating Data – Single epidemic

SARS in 2003 (Worldwide)



*This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.

SARS in 2003 (Toronto)



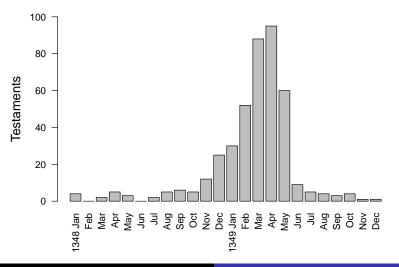
N = 249 (of 250 reported)

Some SARS Facts

High case fatality

- 1918 flu < 3%
- SARS > 10%
- Long hospital stays
 - Mean time from admission to discharge or death: ~ 25 days in Hong Kong
- 8098 probable cases, 774 deaths
- How bad would it have been if it had not been controlled?

The Black Death in London, England, 1348–1349



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London Bill of Mortality, 26 Sept to 3 Oct 1665

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Instructor: David Earn

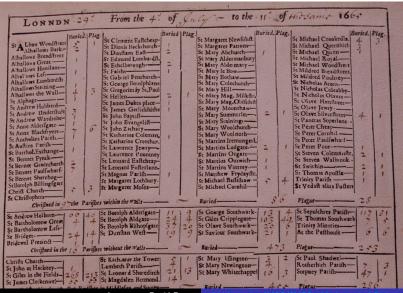
London Bill of Mortality, 26 Sept to 3 Oct 1665

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Instructor: David Earn

1athematics 4MB3/6MB3 Mathematical Biology

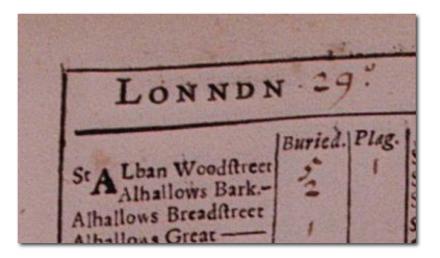
Mortality Bills are typically handwritten



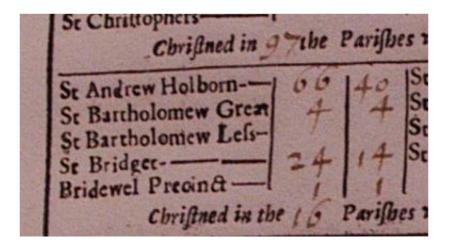
Instructor: David Earn

14/93

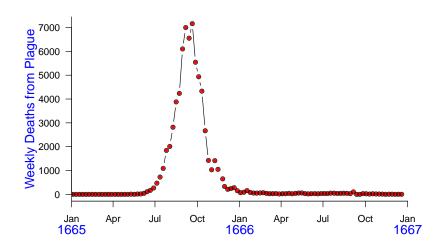
But handwriting is usually very clear



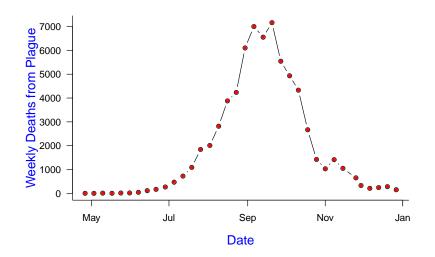
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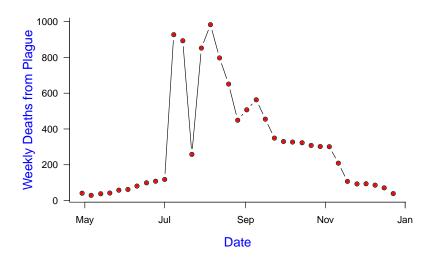
The Great Plague of London, 1665



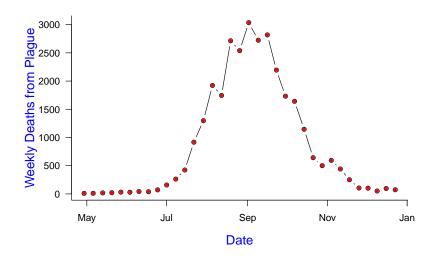
The Great Plague of London, 1665



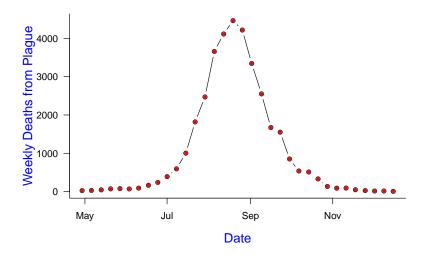
London Plague of 1593



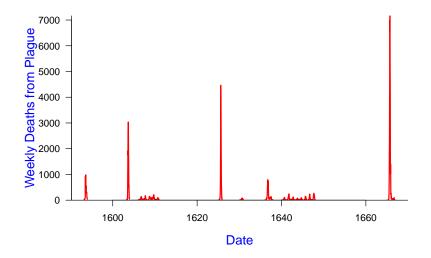
London Plague of 1603



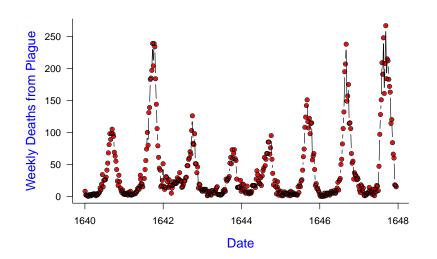
London Plague of 1625



Weekly Deaths from Plague in London, 1592–1666



Weekly Plague in London, 1640–1648



Some Plague Facts

- Plague epidemics recorded from Roman times to early 1900s.
- $\label{eq:last} \mathbf{I}/3 \mbox{ Europe's population died in "Black Death" of 1348} \\ \mathbf{I} \sim 300 \mbox{ years for the population to reach the same level.}$
- Recently (2011) established (at McMaster!) that the pathogen that caused The Black Death was Yersinia pestis

[Bos et al. 2011, Nature 478, 506-510]

 More recently (2014) established (again at McMaster!) that the pathogen that caused The Plague of Justinian (541–543 AD) was *Yersinia pestis*

[Wagner et al. 2014, Lancet Infectious Diseases 14, 319-326]

■ *Y. pestis* still a concern?

Yes: Rodent reservoir, antibiotic-resistant strains, bioterrorism

Spatial data for any plagues? Yes, for London in 1665...

Visualization of spatial structure of Great Plague

- GIS encoding of parish boundaries
- Overlay parish boundaries on more modern map for reference
- Colour parishes as they become infected
- Is there evidence for spatial spread or was the spatial pattern random?
- DE low-tech animation...
- CBC high-tech animation...
 - The Nature of Things, 21 August 2014. http://www.cbc.ca/natureofthings/episodes/ secrets-in-the-bones-the-hunt-for-the-black-death-killer

5 minute Student Respiratory Illness Survey:

https://surveys.mcmaster.ca/limesurvey/index.php/893454

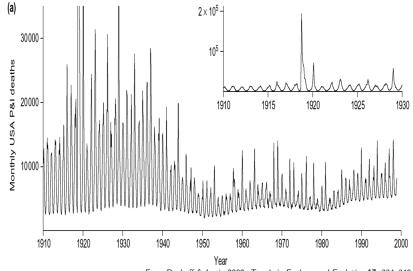
Please complete this anonymous survey to help us monitor the patterns of respiratory illness, over-the-counter drug use, and social contact within the McMaster community. There are no risks to filling out this survey, and your participation is voluntary. You do not need to answer any questions that make you uncomfortable, and all information provided will be kept strictly confidential. Thanks for participating.

-Dr. Marek Smieja (Infectious Diseases)

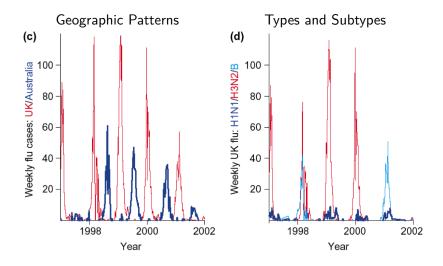
Visualization of entire course of the Great Plague

- What happenned after initial spatial spread?
- Visualize full spatial epidemic structure
- Show magnitude of epidemic in each parish with cylinder.
- Epidemic Visualization (EpiVis) software by Junling Ma.

P&I mortality in U.S.A., 1910–1998



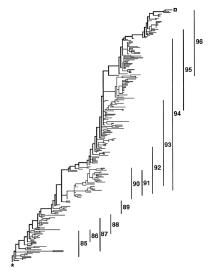
Earn, Dushoff & Levin 2002, Trends in Ecology and Evolution 17, 334-340



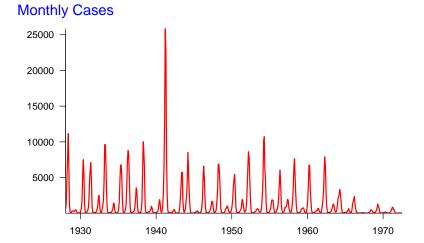
Earn, Dushoff & Levin 2002, Trends in Ecology and Evolution 17, 334-340

Influenza Evolution

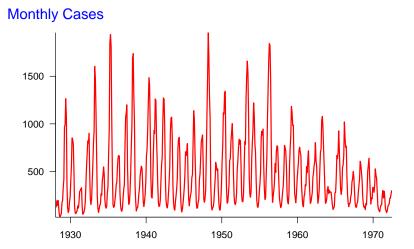
Molecular phylogenetic reconstruction of influenza A/H3N2 evolution, 1985–1996 (Fitch *et al.* 1997)



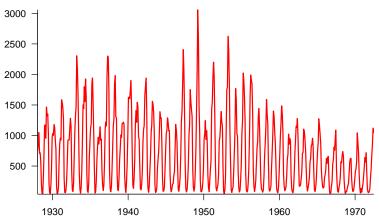
Measles in New York City, 1928–1972



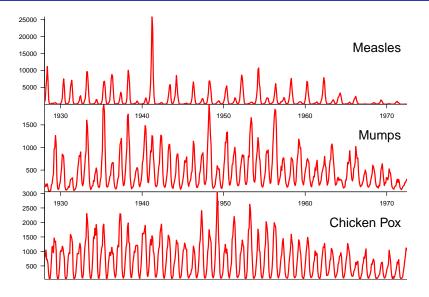
Mumps in New York City, 1928–1972



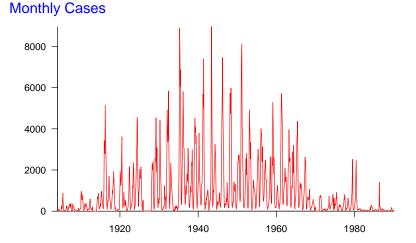




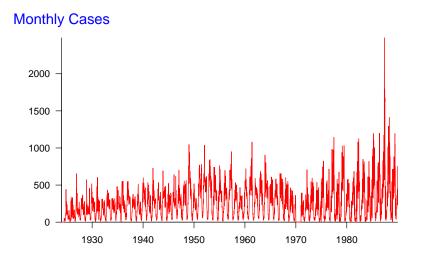
Childhood diseases in New York City, 1928–1972



Measles in Ontario, 1904–1989

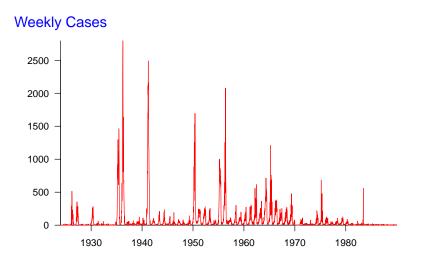


Chicken Pox in Ontario, 1924–1989



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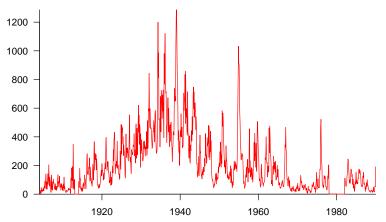
Rubella in Ontario, 1924–1989



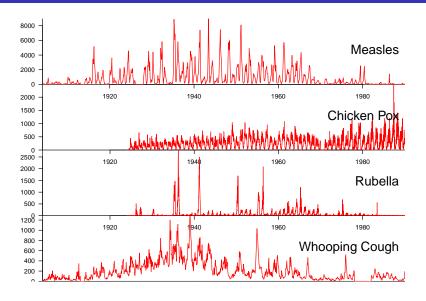
Instructor: David Earn Mathematics 4MB3/6MB3 Mathematical Biology

Whooping Cough in Ontario, 1904–1989





Childhood diseases in Ontario, 1904–1989



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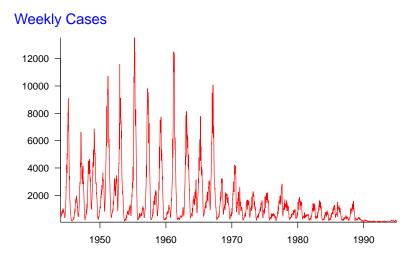
Dominion Bureau of Statistics Disease Notification Data

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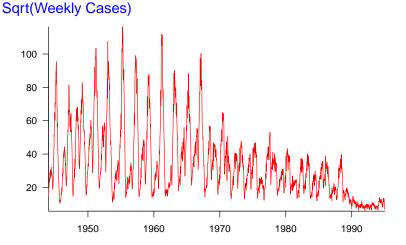
Recurrent epidemics of childhood infections

- Childhood diseases in New York City, 1928–1972
- Childhood diseases in Ontario, 1904–1989

Measles incidence in England and Wales, 1944–1995



Measles incidence in England and Wales, 1944–1995



Why study measles epidemics?

- In 2017, ~ 110,000 deaths from measles
- A major cause of vaccine-preventable deaths.
- Potential impact in developed countries during vaccine scares (e.g., MMR scare in UK in 1990s).
- Understand past patterns
- Predict future patterns
- Manipulate future patterns
- Develop vaccination strategy that can...



Other reasons to model infectious disease epidemics

Mathematical models make hypotheses and inferences precise

- Give better advice to policymakers
- Make better predictions
- Host-pathogen dynamics are important aspects of ecosystem dynamics
 - Infectious disease models more likely to be successful than predator-prey models
- Excellent data for human infectious diseases
 - Models can be tested!

Modelling population dynamics of childhood infections

- The basic SIR model cannot explain recurrent epidemics.
- What should we do?... The usual options:
 - **1** Get depressed, drop the course.
 - 2 Keep developing models until we can explain recurrent epidemics.

 First, let's talk about tools that allow us to make our questions about time series data more precise. 5 minute Student Respiratory Illness Survey:

https://surveys.mcmaster.ca/limesurvey/index.php/893454

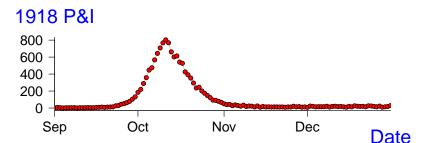
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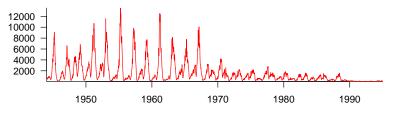
Epidemic Data Analysis

Instructor: David Earn Mathematics 4MB3/6MB3 Mathematical Biology

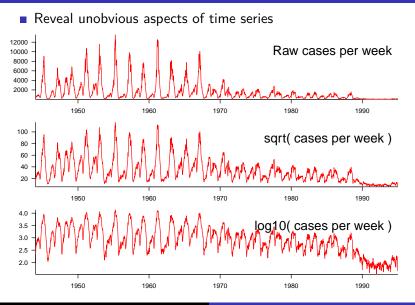
Time Plots of Temporal Epidemic Patterns



Weekly Measles in England and Wales



Time Plots of Transformed Data



- Reveal trends clouded by noise or seasonality
- Moving Average:

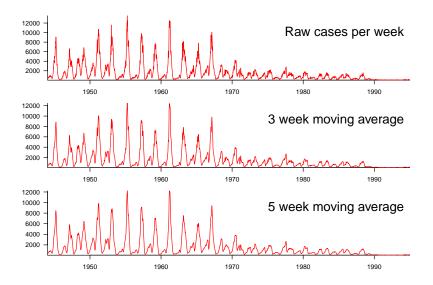
$$x_t \to \frac{1}{2a+1} \sum_{i=-a}^{a} x_{t+i}$$

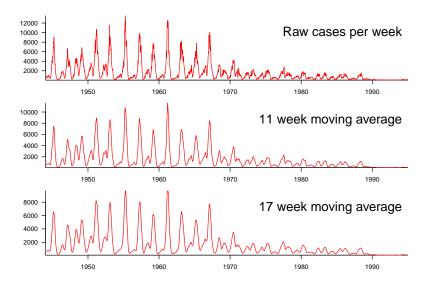
• Replace original data points x_t with averages of nearby points.

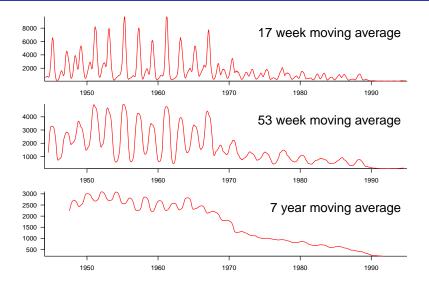
Linear filter:

$$x_t o \sum_{i=-\infty}^{\infty} \lambda_i x_{t+i}$$

- Generalization of moving average.
- Weights λ_i can be nonlinear functions of *i*.







Correlation

- Recurrent epidemics with number of cases in the past and the future.
- Given N pairs of observations of different quantities, {(x_i, y_i) : i = 1,..., N}, the *correlation coefficient* is defined to be

$$r = \frac{\sum_{i=1}^{N} (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{N} (x_i - \bar{x})^2 \sum_{i=1}^{N} (y_i - \bar{y})^2}}$$

where \bar{x} and \bar{y} are the means of $\{x_i\}$ and $\{y_i\}$, respectively.

Correlation

Properties of the correlation coefficient:

- $-1 \le r \le 1$ (Proof? Cauchy-Schwarz inequality)
- r = 1 ⇐⇒ all points lie on a line with positive slope ("complete positive correlation")
- $r = -1 \iff$ all points lie on a line with negative slope ("complete negative correlation")
- $r \simeq 0 \implies$ "uncorrelated"
- Interpretation: r² is the proportion of the variance in y explained by a linear function of x.

Derivations and discussions:

- MathWorld on r^2 , Wikipedia on r^2
- Wikipedia on general coefficient of determination

- Given a single sequence of observations {*x*_t : *t* = 1,...,*N*}, we can compute the correlation of each observation with the observation *k* time steps in the future.
- Thus, we consider the pairs of observations
 {(x_t, x_{k+t}) : t = 1,..., N k} and define the *autocorrelation coefficient at lag k* to be

$$r_{k} = \frac{\sum_{t=1}^{N-k} (x_{t} - \bar{x}_{1,N-k}) (x_{k+t} - \bar{x}_{k+1,N})}{\sqrt{\sum_{t=1}^{N-k} (x_{t} - \bar{x}_{1,N-k})^{2} \sum_{t=1}^{N-k} (x_{k+t} - \bar{x}_{k+1,N})^{2}}}$$

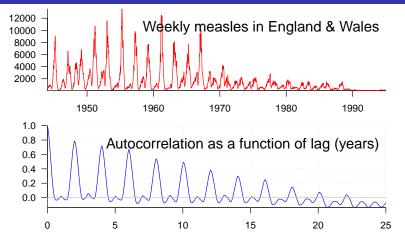
where $\bar{x}_{1,N-k}$ and $\bar{x}_{k+1,N}$ are the means of first and last N-k observations, respectively.

If number of observations N is large and lag $k \ll N$ then

$$r_k \simeq rac{\sum_{t=1}^{N-k} (x_t - ar{x}) (x_{k+t} - ar{x})}{\sum_{t=1}^{N} (x_t - ar{x})^2}$$

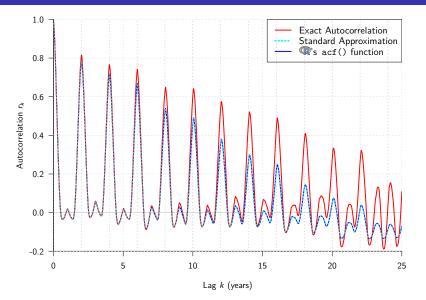
- Approximation of r_k is worse for larger lags k
- Plot of autocorrelation r_k as a function of lag k is called the correlogram.

Correlogram



Peaks in correlogram ⇒ periodicities in original time series.
 Correlograms of temporal segments are often informative.

Correlogram: exact vs. approximate r_k



- Can we compute the dominant periods in the time series? (Rather than estimating them by eye from the correlogram.)
- Express the time series as a Fourier series:

$$x_t = a_0 + \left(\sum_{p=1}^{(N/2)-1} \left(a_p \cos \omega_p t + b_p \sin \omega_p t\right)\right) + a_{N/2} \cos \pi t \,,$$

where $\omega_p = 2\pi p/N$.

Compute the *Fourier coefficients* {a_p}, {b_p} by taking inner products with cos ω_pt and sin ω_pt.

■ Fourier coefficients of *x*_t are:

$$a_0 = \bar{x} = \frac{1}{N} \sum_t x_t ,$$

$$a_p = \frac{2}{N} \sum_t x_t \cos \omega_p t , \qquad b_p = \frac{2}{N} \sum_t x_t \sin \omega_p t ,$$

$$a_{N/2} = \frac{1}{N} \sum_t (-1)^t x_t ,$$

where sum is over observation times.

• Estimated power spectral density (PSD) at frequency ω_p is*:

$$I(\omega_p) = \frac{N}{4\pi} (a_p^2 + b_p^2)$$

*The normalization by $N/4\pi$ is the convention chosen by Chatfield (2004, "Analysis of Time Series: An Introduction"). Other normalization conventions are also in common use.

5 minute Student Respiratory Illness Survey:

https://surveys.mcmaster.ca/limesurvey/index.php/893454

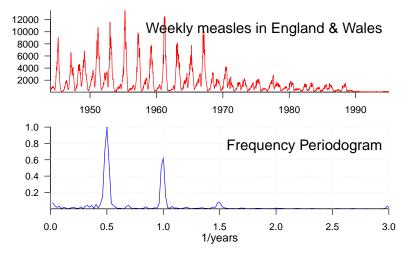
Please complete this anonymous survey to help us monitor the patterns of respiratory illness, over-the-counter drug use, and social contact within the McMaster community. There are no risks to filling out this survey, and your participation is voluntary. You do not need to answer any questions that make you uncomfortable, and all information provided will be kept strictly confidential. Thanks for participating.

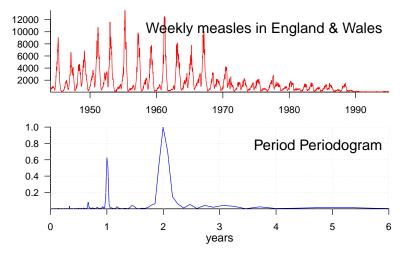
-Dr. Marek Smieja (Infectious Diseases)

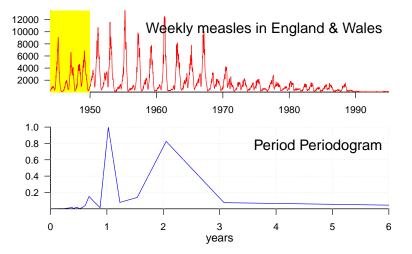
- There are many different ways to express the power spectral density (aka power spectrum).
- Most common/useful equivalence is that the power spectrum is the discrete Fourier transform of the correlogram:

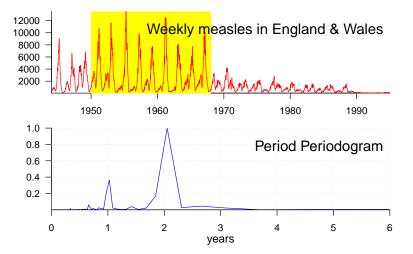
$$I(\omega_p) = \frac{1}{\pi} \left(r_0 + 2 \sum_{k=1}^{N-1} r_k \cos \omega_p k \right)$$

Plot of estimated power spectrum as a function of frequency ω_p is called the *frequency periodogram* or just the *periodogram*.

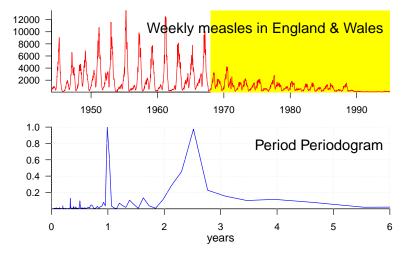


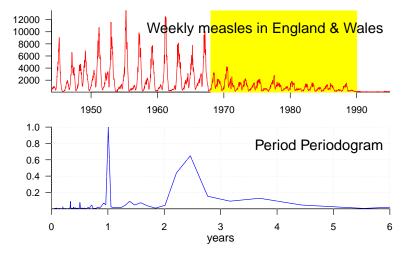






68/93





70/93

Spectral Density Properties

Periodogram is discrete Fourier transform of correlogram

- Same information in correlogram and periodogram
- Periodogram usually easier to interpret
- In Q, calculate power spectrum with spectrum()
- The power spectrum $l(\omega_p)$ partitions the variance in the time series with respect to frequency ω_p .
 - Parseval's theorem implies $\frac{1}{N} \sum_{t} (x_t \bar{x})^2 = \frac{1}{2\pi N} \sum_{p>0} I(\omega_p)$. But $\frac{1}{N} \sum_{t} (x_t - \bar{x})^2 = \text{Var}\{x_t\}$, hence $I(\omega_p)/(2\pi N)$ is the proportion of the variance in the time series associated with period $2\pi/\omega_p$. [For details, see Chatfield (2004).]

Basic Time Series Analysis of Epidemic Data

