McMaster University

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

# Announcements

- 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.

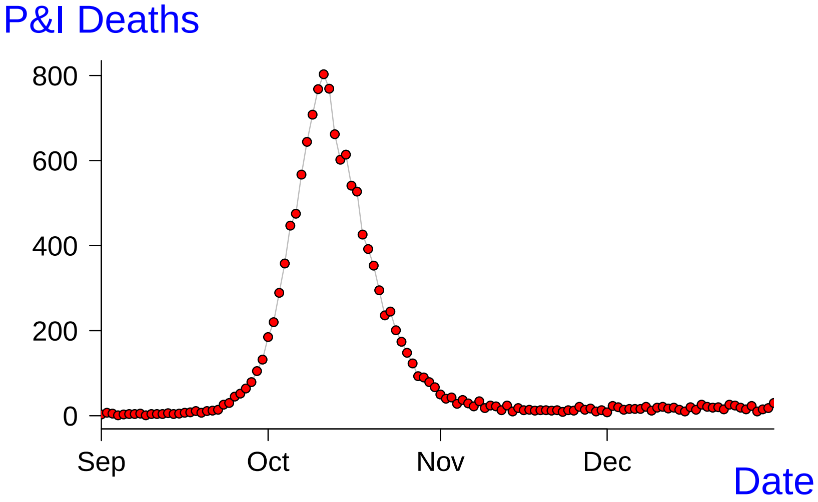
# More Announcements!

- **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

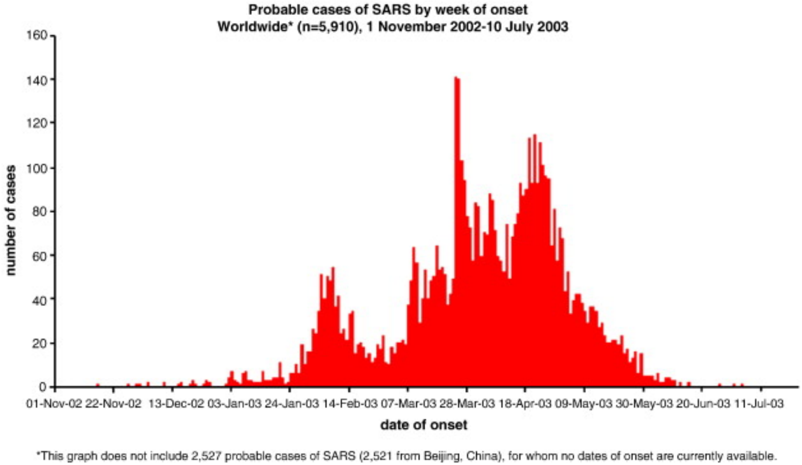
# Attendance

Who is here?

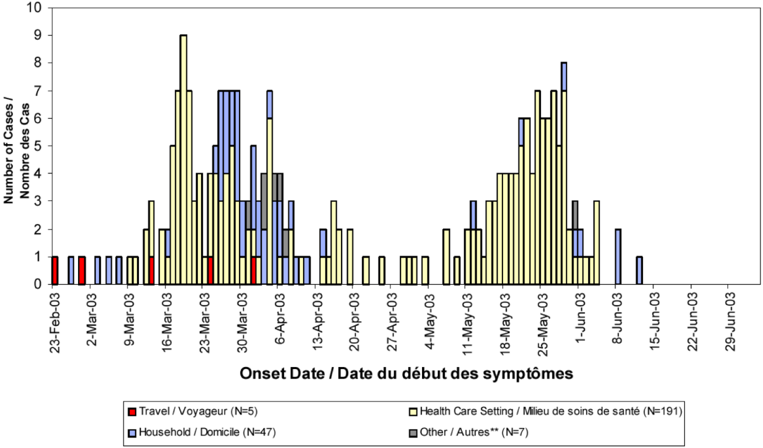
# P&I Mortality, Philadelphia, 1918



# SARS in 2003 (Worldwide)



# SARS in 2003 (Toronto)

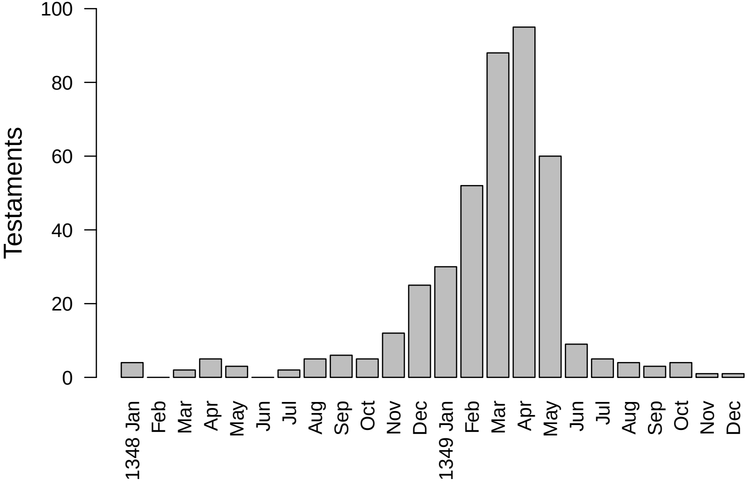



$N = 249$ (of 250 reported)

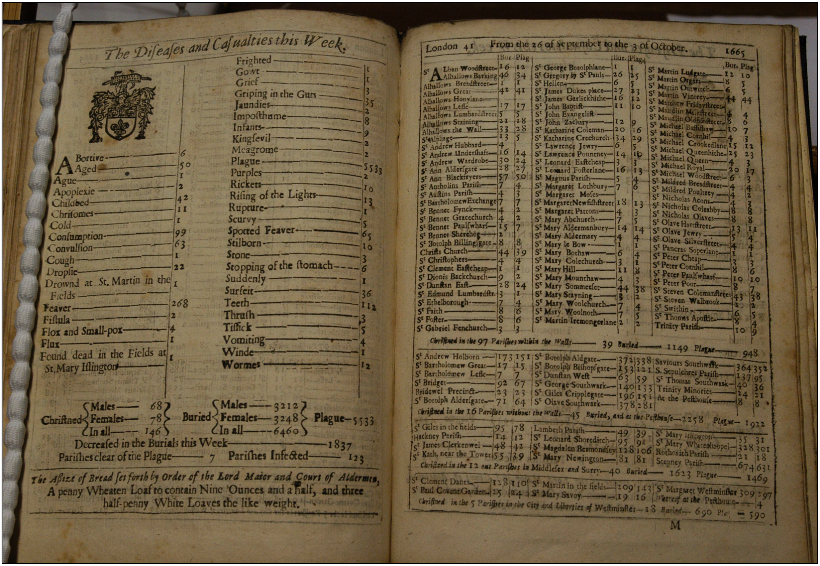
# Some SARS Facts

- High case fatality
  - 1918 flu $< 3\%$
  - SARS $> 10\%$
- Long hospital stays
  - Mean time from admission to discharge or death: $\sim 25$ 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



# London Bill of Mortality, 26 Sept to 3 Oct 1665



*The Diseases and Casualties this Week.*

| | |
|---|---|
| Bortive | 6 |
| Aged | 50 |
| Ague | 1 |
| Apoplexie | 2 |
| Childbed | 42 |
| Chrisomes | 11 |
| Cold | 1 |
| Consumption | 99 |
| Convulsion | 63 |
| Cough | 1 |
| Dropsie | 22 |
| Drownd at St. Martin in the Fields | 1 |
| Feaver | 268 |
| Fistula | 2 |
| Flox and Small-pox | 4 |
| Flux | 1 |
| Found dead in the Fields at St. Mary Islington | 1 |
| Frighted | 1 |
| Gowt | 1 |
| Grief | 1 |
| Griping in the Guts | 35 |
| Jaundies | 2 |
| Impostume | 8 |
| Infants | 9 |
| Kingsevil | 2 |
| Meagrome | 2 |
| Plague | 5533 |
| Purples | 2 |
| Rickets | 10 |
| Rising of the Lights | 13 |
| Rupture | 1 |
| Scurvy | 5 |
| Spotted Feaver | 65 |
| Stilborn | 10 |
| Stone | 3 |
| Stopping of the stomach | 6 |
| Suddenly | 1 |
| Surfeit | 36 |
| Teeth | 112 |
| Thrush | 3 |
| Tissick | 5 |
| Vomiting | 4 |
| Winde | 1 |
| Wormes | 12 |

Christned: Males 68, Females 78, In all 146
Buried: Males 3212, Females 3248, In all 6460
Plague 5533

Decreased in the Burials this Week 1837

Parishes clear of the Plague 7    Parishes Infected 123

*The Assize of Bread set forth by Order of the Lord Maior and Court of Aldermen,* A penny Wheaten Loaf to contain Nine Ounces and a half, and three half-penny White Loaves the like weight.

London 41    From the 26 of September to the 3 of October.    1665

Christned in the 97 Parishes within the Walls 39   Buried 1149   Plague 948

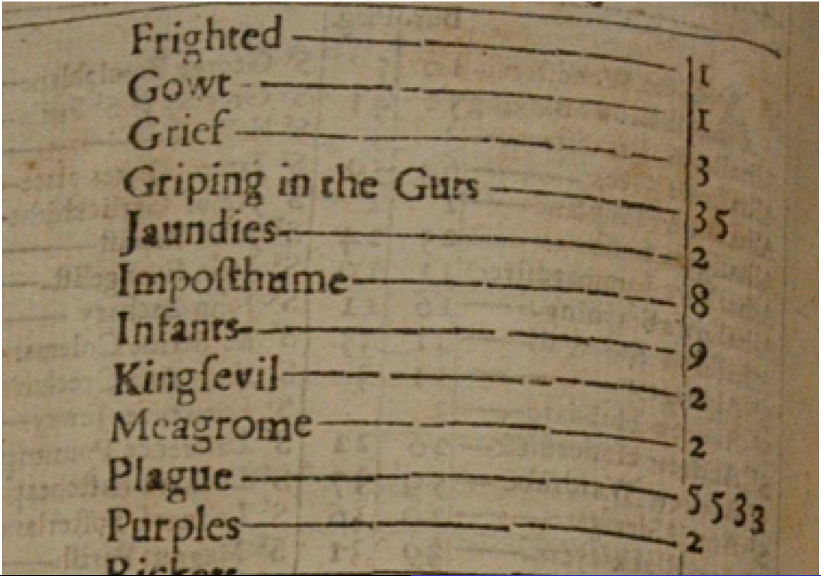
Christned in the 16 Parishes without the Walls 45   Buried, and at the Pesthouse 2258   Plague 1922

Christned in the 12 out Parishes in Middlesex and Surry 40   Buried 1623   Plague 1469

Christned in the 5 Parishes in the City and Liberties of Westminster 18   Buried 690   Plague 590

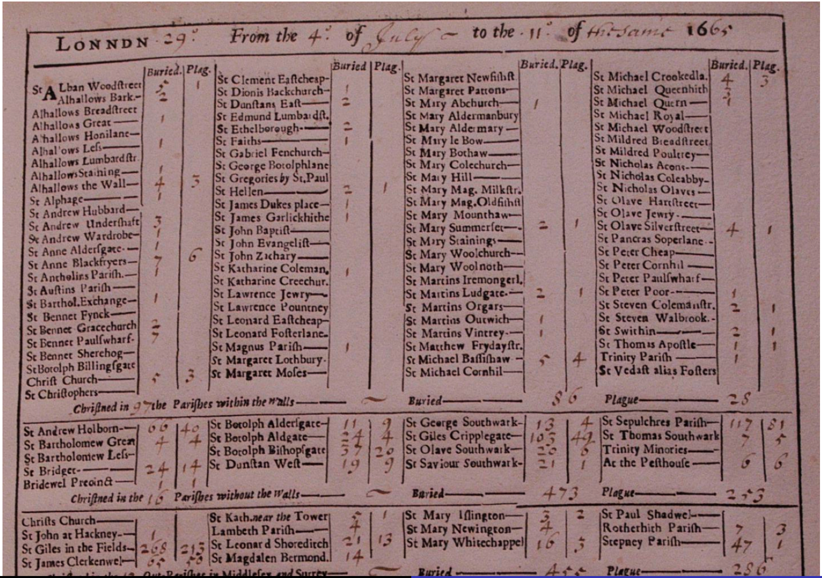
M

# London Bill of Mortality, 26 Sept to 3 Oct 1665



| | |
|---|---|
| Frighted | 1 |
| Gowt | 1 |
| Grief | 3 |
| Griping in the Guts | 35 |
| Jaundies | 2 |
| Impoſthume | 8 |
| Infants | 9 |
| Kingſevil | 2 |
| Meagrome | 2 |
| Plague | 5533 |
| Purples | 2 |

# Mortality Bills are typically handwritten



LONNDN 29° From the 4° of July — to the 11° of the same 1665

| Parish | Buried. | Plag. | Parish | Buried | Plag. | Parish | Buried. | Plag. | Parish | Buried. | Plag. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| St Alban Woodstreet | 5 | 1 | St Clement Eastcheap |  |  | St Margaret Newfishst |  |  | St Michael Crookedla. | 4 | 3 |
| Alhallows Bark. | 2 |  | St Dionis Backchurch | 1 |  | St Margaret Pattons |  |  | St Michael Queenhith | 3 |  |
| Alhallows Breadstreet |  |  | St Dunstans East | 2 |  | St Mary Abchurch | 1 |  | St Michael Quern | 1 |  |
| Alhallows Great | 1 |  | St Edmund Lumbardst. |  |  | St Mary Aldermanbury |  |  | St Michael Royal |  |  |
| Alhallows Honilane |  |  | St Ethelborough | 2 |  | St Mary Aldermary |  |  | St Michael Woodstreet |  |  |
| Alhallows Less | 1 |  | St Faiths | 1 |  | St Mary le Bow |  |  | St Mildred Breadstreet |  |  |
| Alhallows Lumbardstr. |  |  | St Gabriel Fenchurch |  |  | St Mary Bothaw |  |  | St Mildred Poultrey |  |  |
| Alhallows Staining | 1 |  | St George Botolphlane |  |  | St Mary Colechurch |  |  | St Nicholas Acons |  |  |
| Alhallows the Wall | 4 | 3 | St Gregories by St. Paul |  |  | St Mary Hill |  |  | St Nicholas Coleabby |  |  |
| St Alphage | 1 |  | St Hellen | 2 | 1 | St Mary Mag. Milkstr. |  |  | St Nicholas Olaves |  |  |
| St Andrew Hubbard |  |  | St James Dukes place | 1 |  | St Mary Mag. Oldfishst |  |  | St Olave Hartstreet |  |  |
| St Andrew Undershaft | 3 |  | St James Garlickhithe | 1 |  | St Mary Mounthaw |  |  | St Olave Jewry |  |  |
| St Andrew Wardrobe | 1 |  | St John Baptist |  |  | St Mary Summerset | 2 | 1 | St Olave Silverstreet | 4 | 1 |
| St Anne Aldersgate | 1 |  | St John Evangelist |  |  | St Mary Stainings |  |  | St Pancras Soperlane |  |  |
| St Anne Blackfryers | 7 | 6 | St John Zachary |  |  | St Mary Woolchurch |  |  | St Peter Cheap |  |  |
| St Antholins Parish. | 1 |  | St Katharine Coleman | 1 |  | St Mary Woolnoth |  |  | St Peter Cornhil |  |  |
| St Austins Parish |  |  | St Katharine Creechur. |  |  | St Martins Iremongerl. |  |  | St Peter Paulswharf |  |  |
| St Barthol. Exchange | 1 |  | St Lawrence Jewry |  |  | St Martins Ludgate | 2 | 1 | St Peter Poor | 1 |  |
| St Bennet Fynck |  |  | St Lawrence Pountney |  |  | St Martins Orgars |  |  | St Steven Colemanstr. | 2 | 1 |
| St Bennet Gracechurch | 2 |  | St Leonard Eastcheap |  |  | St Martins Outwich | 1 |  | St Steven Walbrook. |  |  |
| St Bennet Paulswharf | 7 |  | St Leonard Fosterlane. |  |  | St Martins Vintrey | 1 |  | St Swithin | 2 | 1 |
| St Bennet Sherehog |  |  | St Magnus Parish | 1 |  | St Matthew Frydaystr. |  |  | St Thomas Apostle | 1 | 1 |
| St Botolph Billingsgate |  |  | St Margaret Lothbury |  |  | St Michael Bassishaw | 5 | 4 | Trinity Parish | 1 |  |
| Christ Church | 5 | 3 | St Margaret Moses |  |  | St Michael Cornhil |  |  | St Vedast alias Fosters |  |  |
| St Christophers |  |  |  |  |  |  |  |  |  |  |  |

Christned in 97 the Parishes within the Walls — Buried — 86 Plague — 28

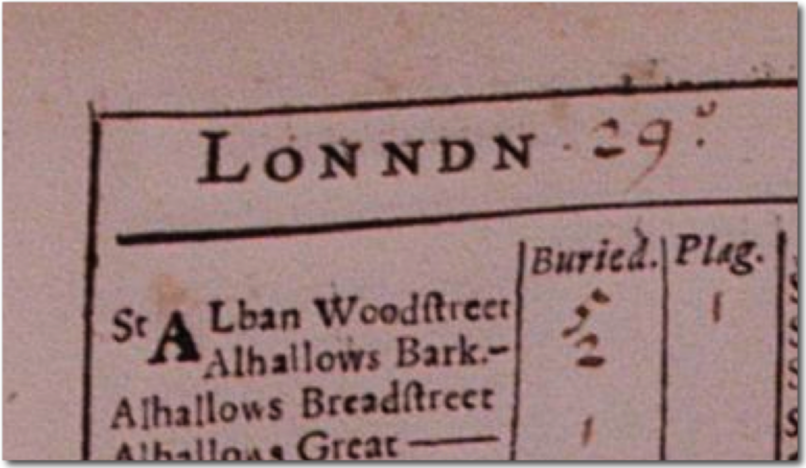
| Parish | Buried | Plag. | Parish | Buried | Plag. | Parish | Buried | Plag. | Parish | Buried | Plag. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| St Andrew Holborn | 66 | 40 | St Botolph Aldersgate | 11 | 9 | St George Southwark | 13 | 4 | St Sepulchres Parish | 117 | 81 |
| St Bartholomew Great | 4 | 4 | St Botolph Aldgate | 24 | 4 | St Giles Cripplegate | 103 | 49 | St Thomas Southwark | 7 | 5 |
| St Bartholomew Less |  |  | St Botolph Bishopsgate | 37 | 20 | St Olave Southwark | 20 | 6 | Trinity Minories |  |  |
| St Bridget | 24 | 14 | St Dunstan West | 19 | 9 | St Saviour Southwark | 21 | 1 | At the Pesthouse | 6 | 6 |
| Bridewel Precinct | 1 | 1 |  |  |  |  |  |  |  |  |  |

Christned in the 16 Parishes without the Walls — Buried — 473 Plague — 253

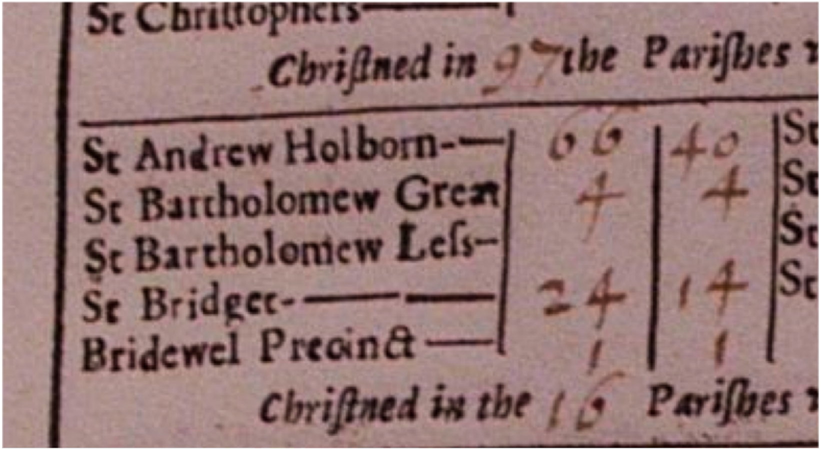
| Parish | Buried | Plag. | Parish | Buried | Plag. | Parish | Buried | Plag. | Parish | Buried | Plag. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Christs Church |  |  | St Kath. near the Tower | 5 | 1 | St Mary Islington | 3 | 2 | St Paul Shadwel |  |  |
| St John at Hackney | 1 |  | Lambeth Parish | 4 |  | St Mary Newington | 4 |  | Rotherhith Parish | 7 | 3 |
| St Giles in the Fields | 268 | 213 | St Leonard Shoreditch | 21 | 13 | St Mary Whitechappel | 16 | 3 | Stepney Parish | 47 | 1 |
| St James Clerkenwel | 65 | 50 | St Magdalen Bermond. | 14 |  |  |  |  |  |  |  |

Out-Parishes in Middlesex and Surrey — Buried — 455 Plague — 256

# But handwriting is usually very clear



# But handwriting is usually very clear



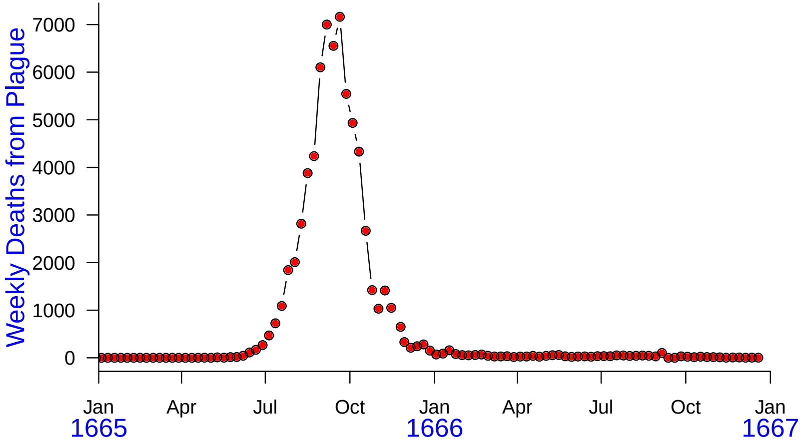
St Chriſtophers———

*Chriſtned in 97 the Pariſhes*

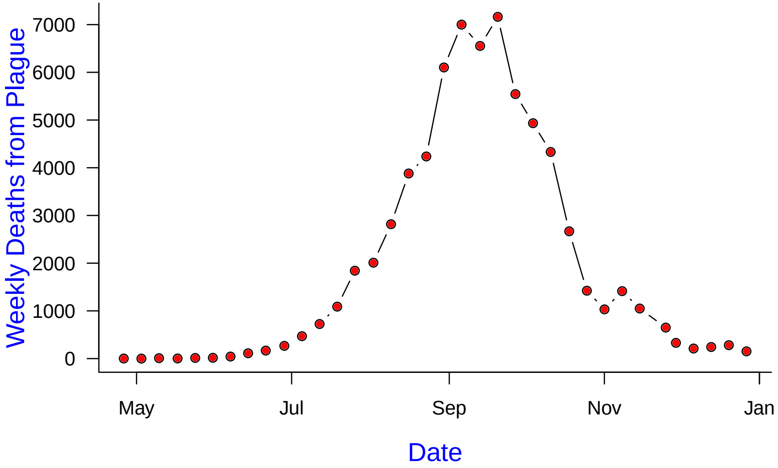
| | | | |
|---|---|---|---|
| St Andrew Holborn—— | 66 | 40 | St |
| St Bartholomew Great | 4 | 4 | St |
| St Bartholomew Leſs— | | | St |
| St Bridget———— | 24 | 14 | St |
| Bridewel Precinct—— | 1 | 1 | |

*Chriſtned in the 16 Pariſhes*

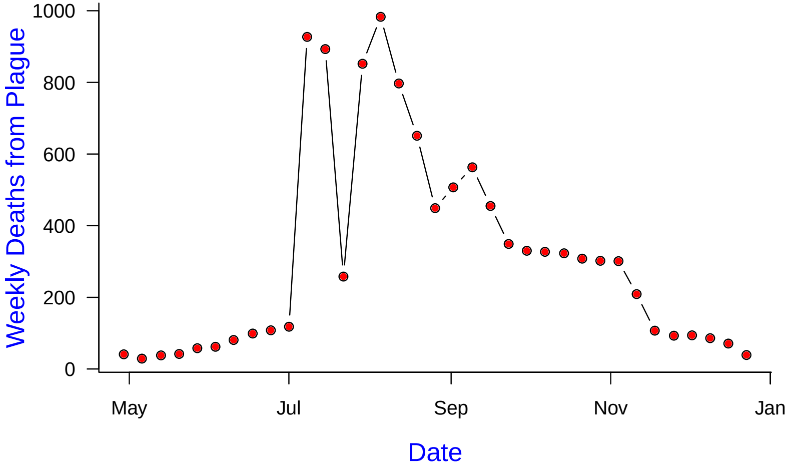
# The Great Plague of London, 1665



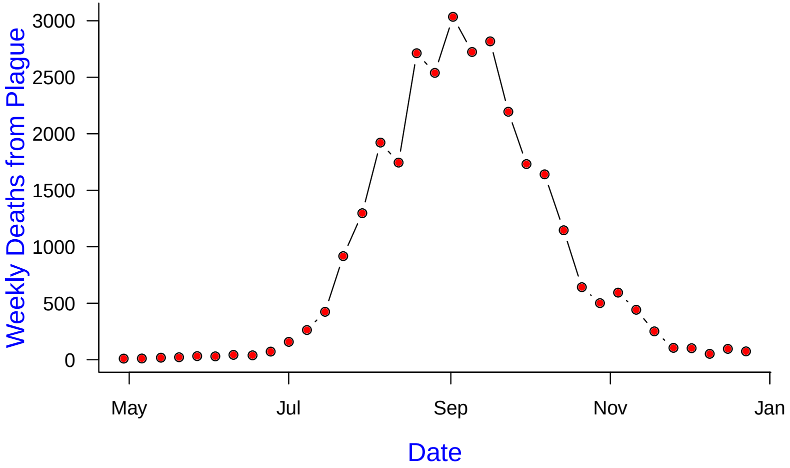
# The Great Plague of London, 1665



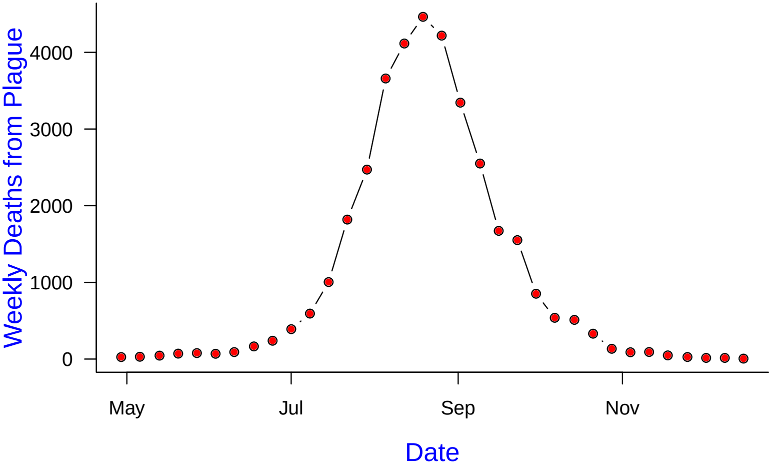
# London Plague of 1593



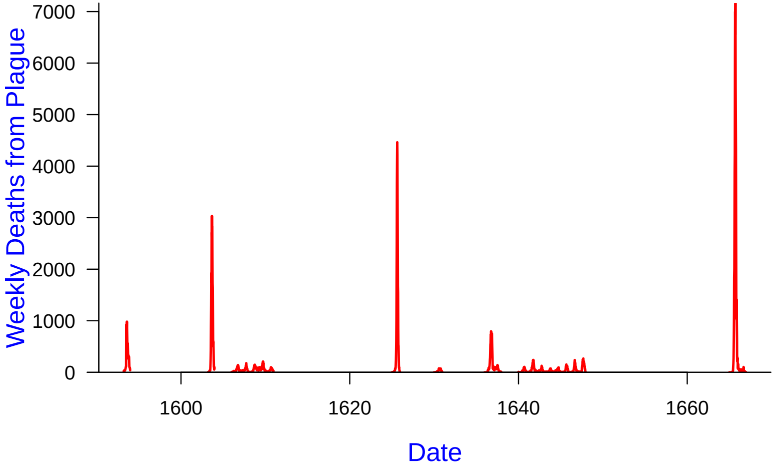
# London Plague of 1603



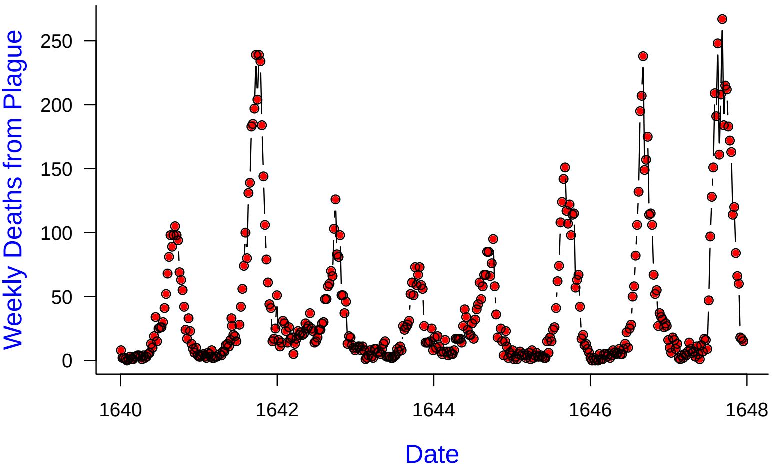
# London Plague of 1625



# 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.
- $\gtrsim 1/3$ Europe's population died in "Black Death" of 1348
  - $\sim 300$ 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

# Please consider. . .

**5 minute** *Student Respiratory Illness Survey:*

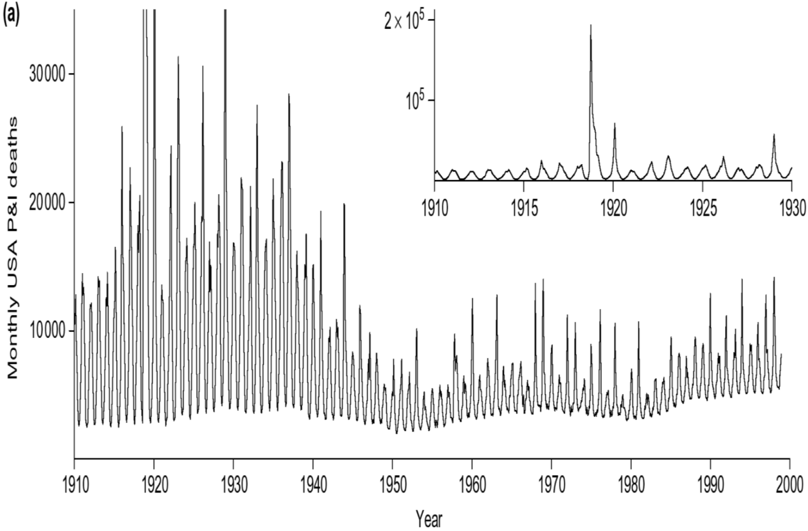
https://surveys.mcmaster.ca/limesurvey/index.php/893454

> *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

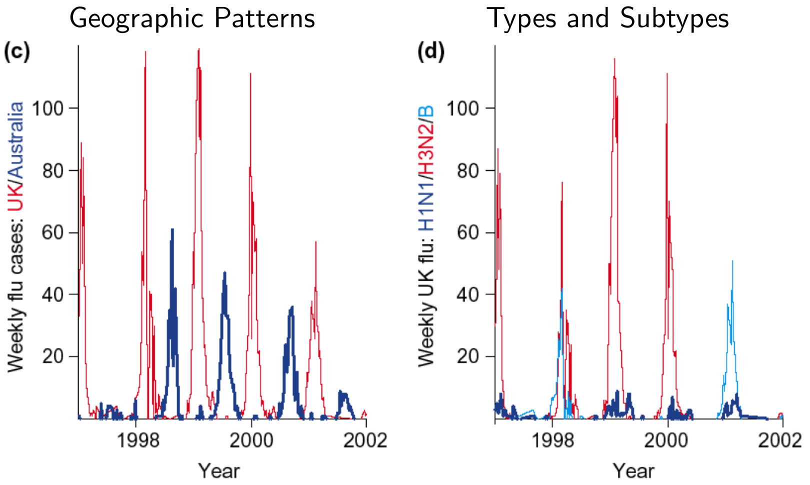
- What happenned after initial spatial spread?
- Visualize full spatial epidemic structure
- Show magnitude of epidemic in each parish with cylinder.
- Epidemic Visualization (`EpiVis`) software by Junling Ma.

# P&I mortality in U.S.A., 1910–1998




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

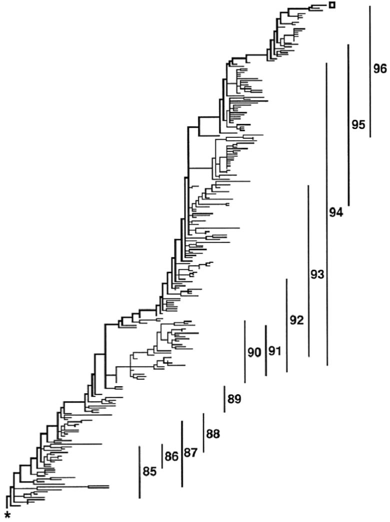
# Influenza Incidence Patterns (lab confirmed)



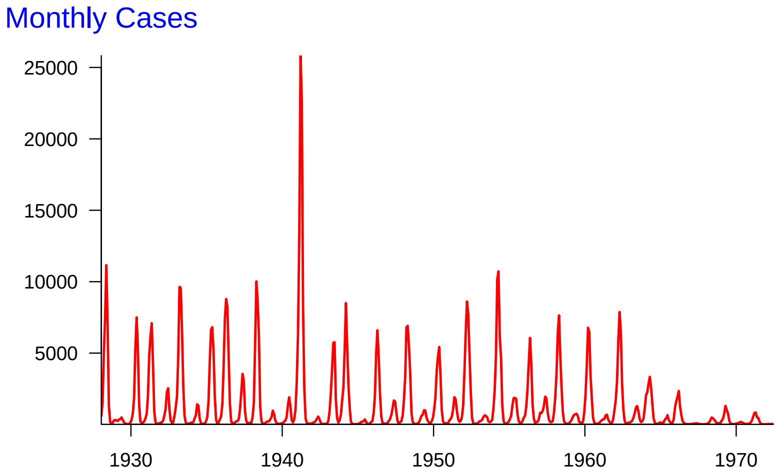

Earn, Dushoff & Levin 2002, *Trends in Ecology and Evolution* **17**, 334–340

# Influenza Evolution

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

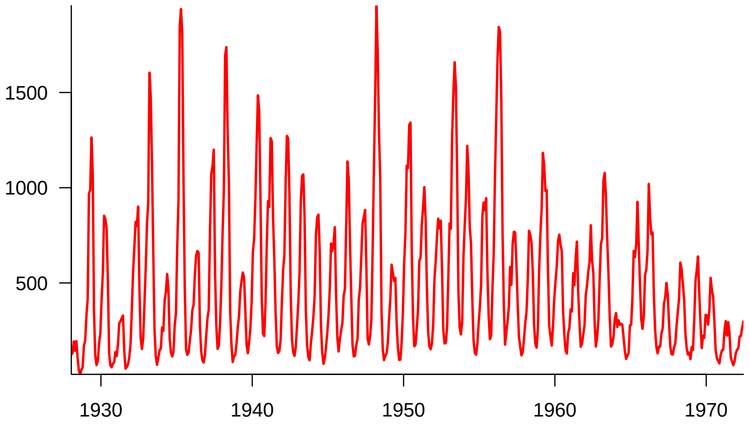


# Measles in New York City, 1928–1972



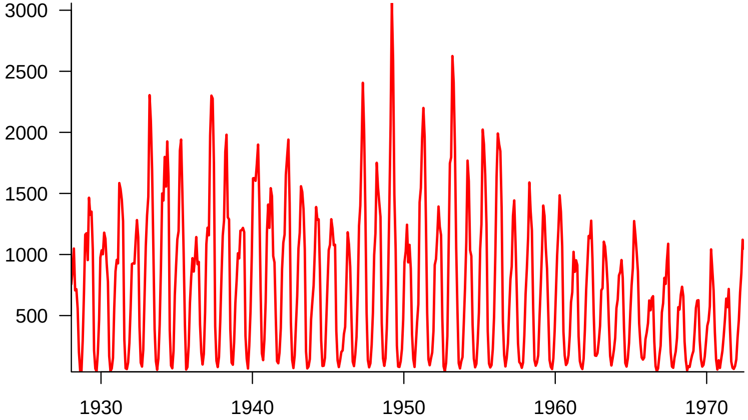
# Mumps in New York City, 1928–1972

## Monthly Cases

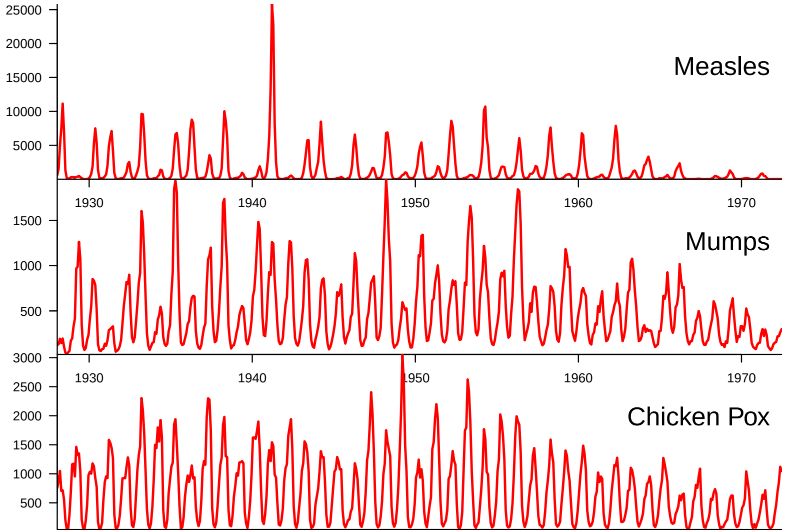


# Chicken Pox in New York City, 1928–1972

Monthly Cases

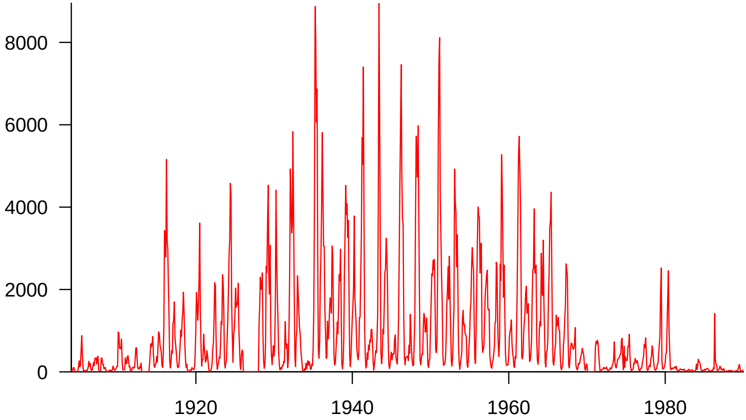


# Childhood diseases in New York City, 1928–1972



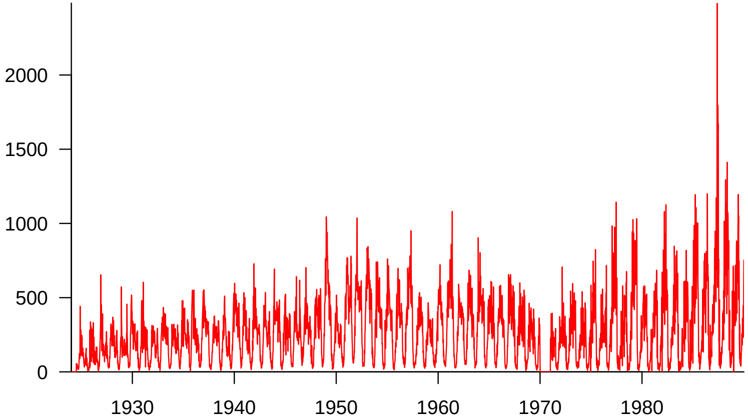
# Measles in Ontario, 1904–1989

## Monthly Cases

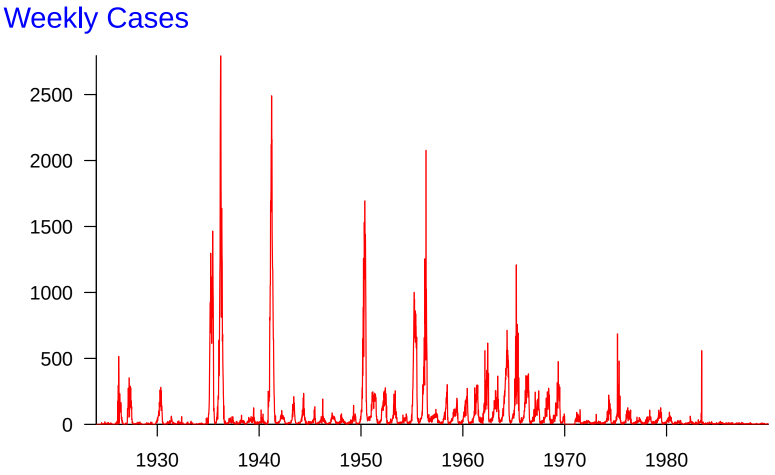


# Chicken Pox in Ontario, 1924–1989

## Monthly Cases

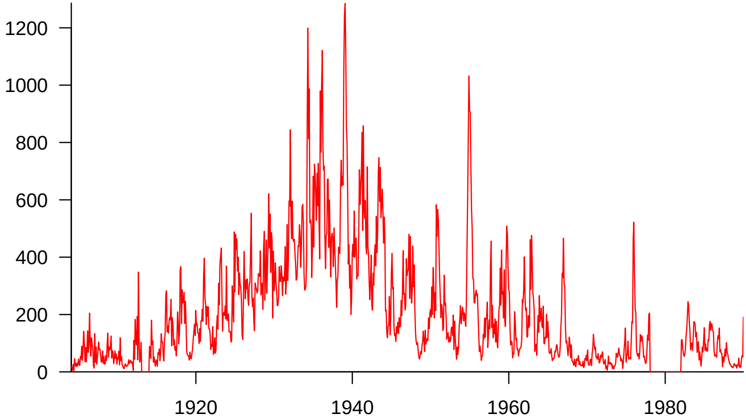


# Rubella in Ontario, 1924–1989

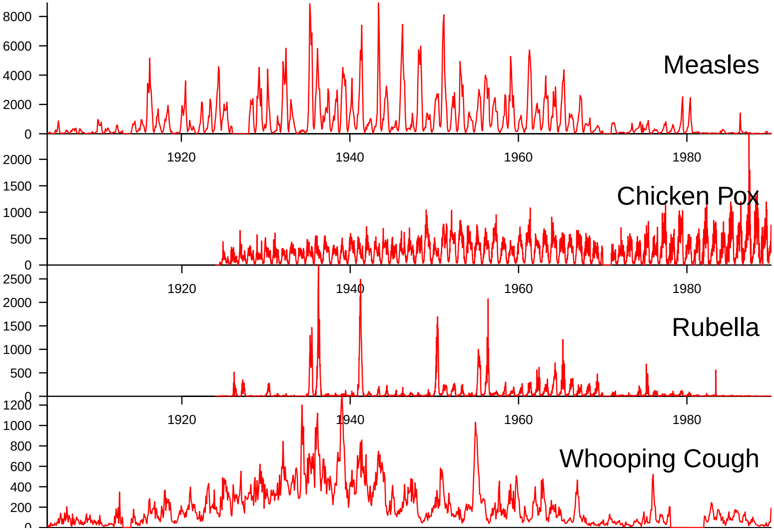


# Whooping Cough in Ontario, 1904–1989

## Monthly Cases



# Childhood diseases in Ontario, 1904–1989



# Ontario Disease Notification Data

Province of O

YEAR: 1939 COUNTY........ MUNICIPALITY........

| Month | Week End. | | CSM C | CSM D | C.P. C | C.P. D | DIP. C | DIP. D | DYS. A/B C | DYS. A/B D | EN. LETH. C | EN. LETH. D | ERYS. C | ERYS. D | G.C. C | G.C. D | FLU. C | FLU. D | INF. JAUN. C | INF. JAUN. D | G.M. C | G.M. D | MEAS. C | MEAS. D | MUMPS C | MUMPS D | PARA. TYPH. C | PARA. TYPH. D |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Jan. | 7 | 1 | | | 452 | 1 | 3 | 0 | 1 | 0 | | | 5 | 1 | 101 | 0 | 8 | 1 | 17 | 0 | 17 | 0 | 670 | 1 | 56 | 0 | 2 | 0 |
| | 14 | 2 | 2 | 1 | 490 | 0 | 8 | 0 | | | | | 5 | 0 | 82 | 0 | 21 | 1 | 18 | 0 | 18 | 0 | 850 | 0 | 92 | 0 | 1 | 0 |
| | 21 | 3 | 2 | 1 | 511 | 0 | 9 | 3 | | | 0 | 1 | 5 | 0 | 89 | 0 | 16 | 2 | 26 | 0 | 22 | 0 | 932 | 0 | 98 | 0 | | |
| | 28 | 4 | 1 | 0 | 384 | 0 | 2 | 0 | | | | | 2 | 0 | 73 | 0 | 164 | 0 | 10 | 0 | 28 | 0 | 933 | 1 | 24 | 0 | | |
| | Total | | 5 | 2 | 1837 | 1 | 22 | 3 | 1 | 0 | 0 | 1 | 17 | 1 | 345 | 0 | 209 | 4 | 71 | 0 | 85 | 0 | 3385 | 2 | 270 | 0 | 3 | 0 |
| Feb. | 4 | 5 | | | 355 | 0 | 7 | 1 | 1 | 0 | | | 3 | 0 | 83 | 0 | 57 | 1 | 24 | 0 | 25 | 0 | 1335 | 1 | 110 | 0 | 2 | 0 |
| | 11 | 6 | 2 | 1 | 363 | 0 | 1 | 0 | 1 | 0 | | | 7 | 0 | 82 | 0 | 27 | 1 | 41 | 1 | 29 | 0 | 1033 | 0 | 91 | 0 | 1 | 0 |
| | 18 | 7 | 2 | 1 | 354 | 1 | 2 | 0 | | | | | 4 | 1 | 68 | 0 | 103 | 1 | 35 | 0 | 44 | 0 | 1161 | 0 | 59 | 0 | | |
| | 25 | 8 | 1 | 1 | 308 | 0 | 2 | 0 | | | | | 9 | 0 | 56 | 0 | 177 | 0 | 19 | 0 | 28 | 0 | 999 | 0 | 73 | 0 | | |
| | Total | | 5 | 3 | 1380 | 1 | 12 | 1 | 2 | 0 | | | 23 | 1 | 289 | 0 | 364 | 3 | 119 | 1 | 126 | 0 | 4528 | 1 | 333 | 0 | 3 | 0 |
| Mar. | 4 | 9 | 1 | 1 | 271 | 0 | 7 | 1 | 3 | 1 | | | 7 | 0 | 93 | 0 | 1114 | 19 | 21 | 0 | 40 | 0 | 1131 | 2 | 109 | 0 | 1 | 0 |
| | 11 | 10 | | | 239 | 0 | 7 | 0 | 2 | 0 | | | 8 | 1 | 61 | 0 | 1371 | 8 | 31 | 0 | 32 | 0 | 845 | 0 | 91 | 0 | 2 | 0 |
| | 18 | 11 | | | 166 | 0 | | | | | | | 6 | 0 | 66 | 0 | 1322 | 6 | 5 | 0 | 59 | 0 | 969 | 2 | 69 | 0 | 1 | 0 |
| | 25 | 12 | 1 | 2 | 236 | 0 | 1 | 0 | 1 | 0 | | | 7 | 0 | 63 | 0 | 806 | 16 | 9 | 0 | 20 | 0 | 879 | 0 | 120 | 0 | [illegible] | |
| | Total | | 2 | 3 | 912 | 0 | 15 | 1 | 6 | 1 | | | 28 | 1 | 283 | 0 | 4613 | 49 | 66 | 0 | 151 | 0 | 3824 | 4 | 389 | 0 | 3 | 0 |
| Apr. | 1 | 13 | 2 | 0 | 139 | 0 | 3 | 0 | 1 | 0 | | | 8 | 0 | 95 | 0 | 667 | 6 | 1 | 0 | 24 | 0 | 950 | 0 | 89 | 0 | 3 | 0 |
| | 8 | 14 | 2 | 0 | 162 | 0 | 1 | 0 | 1 | 0 | | | 5 | 0 | 67 | 0 | 731 | 22 | | | 14 | 0 | 790 | 0 | 65 | 0 | 1 | 0 |
| | 15 | 15 | 2 | 0 | 108 | 0 | 1 | 0 | | | 0 | 1 | 11 | 0 | 41 | 0 | 529 | 16 | 2 | 0 | 16 | 0 | 745 | 0 | 56 | 0 | | |
| | 22 | 16 | 1 | 1 | 134 | 0 | 2 | 0 | 1 | 0 | 1 | 1 | 6 | 0 | 64 | 0 | 245 | 8 | 2 | 0 | 26 | 0 | 845 | 0 | 54 | 0 | | |
| | 29 | 17 | 5 | 1 | 167 | 0 | 4 | 0 | 2 | 0 | 2 | 1 | 3 | 0 | 55 | 0 | 124 | 9 | 2 | 1 | 13 | 0 | 746 | 1 | 120 | 0 | | |
| | Total | | 12 | 2 | 710 | 0 | 11 | 0 | 5 | 0 | 3 | 3 | 33 | 0 | 322 | 0 | 2296 | 61 | 7 | 1 | 93 | 0 | 4076 | 1 | 384 | 0 | 4 | 0 |
| | 6 | 18 | 2 | 0 | 104 | 0 | 1 | 0 | 2 | 0 | | | 4 | 0 | 71 | 0 | 76 | 3 | 1 | 0 | 14 | 0 | 877 | 0 | 63 | 0 | 3 | 0 |

# Dominion Bureau of Statistics Disease Notification Data

VITAL STATISTICS BRANCH - COMMUNICABLE DISEASE SECTION

Cases of Whooping Cough Reported by Provincial Health Departments, Year 1924

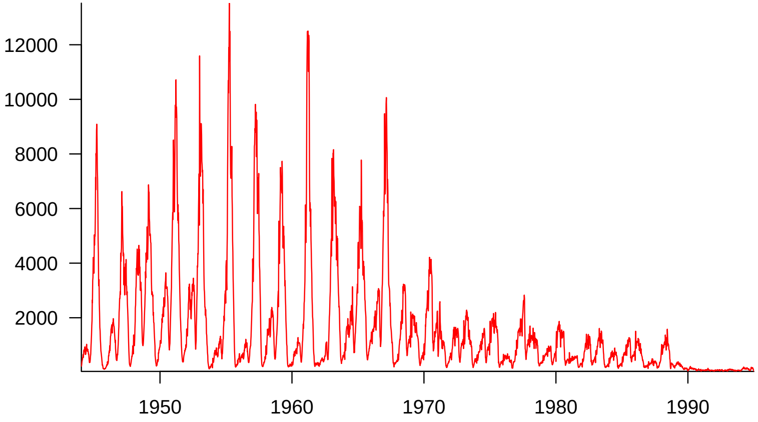
| WEEK ENDING | P.E.I. | | N.S. | | N.B. | | QUE. | | ONT. | | MAN. | | SASK. | | ALTA. | | B.C. | | CANADA | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | wk | mt | wk | mt | wk | mt | wk | mt | wk | mt | wk | mt | wk | mt | wk | mt | wk | mt | wk | mt |
| 1 JAN 5 | | | 11 | | | | | | | | | | 1 | | | | | | 12 | |
| 2 12 | | | 29 | | | | | | | | | | 18 | | | | | | 47 | |
| 3 19 | | | 37 | | | | | | | | | | 32 | | | | | | 69 | |
| 4 26 | | | 75 | 152 | | | | 68 | | 181 | | 36 | 13 | 64 | | 97 | | 4 | 88 | 602 |
| 5 FEB 2 | | | 12 | | 1 | | | | | | | | 53 | | | | | | 66 | |
| 6 9 | | | 5 | | | | | | | | | | 40 | | | | | | 45 | |
| 7 16 | | | 31 | | | | | | | | | | 14 | | | | | | 45 | |
| 8 23 | | | -2 | 50 | 1 | 2 | | 267 | | 202 | | 48 | 4 | 111 | | 116 | | 1 | 7 | 797 |
| 9 MAR 1 | | | 2 | | | | | | | | | | 21 | | | | | | 23 | |
| 10 8 | | | | | | | | | | | | | 9 | | | | | | 9 | |
| 11 15 | | | 3 | | | | | | | | | | 11 | | | | | | 14 | |
| 12 22 | | | 60 | | | | | | | | | | 34 | | | | | | 94 | |
| 13 29 | | | 2 | 61 | | | | 144 | | 140 | | 52 | 15 | 90 | | 15 | | 7 | 17 | 515 |
| 14 APR 5 | | | 9 | | | | | | | | | | 11 | | | | | | 20 | |
| 15 12 | | | 1 | | | | | | | | | | 12 | | | | | | 13 | |
| 16 19 | | | 26 | | 1 | | | | | | | | 8 | | | | | | 35 | |
| 17 26 | | | 14 | 50 | 3 | 4 | | 42 | | 140 | | 39 | 16 | 47 | | 67 | | 5 | 33 | 394 |
| 18 MAY 3 | | | 26 | | | | | | | | | | 2 | | | | | | 28 | |

# Recurrent epidemics of childhood infections

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

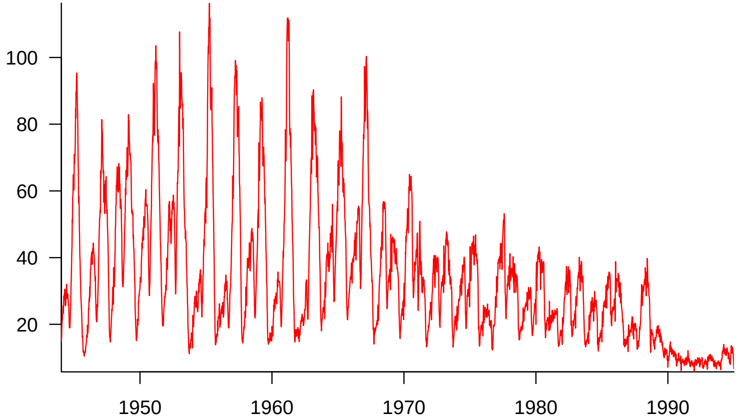
# Measles incidence in England and Wales, 1944–1995

## Weekly Cases



# Measles incidence in England and Wales, 1944–1995

Sqrt(Weekly Cases)



# Why study measles epidemics?

- In 2017, $\sim 110,000$ 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.

# Please consider...

**5 minute** *Student Respiratory Illness Survey:*

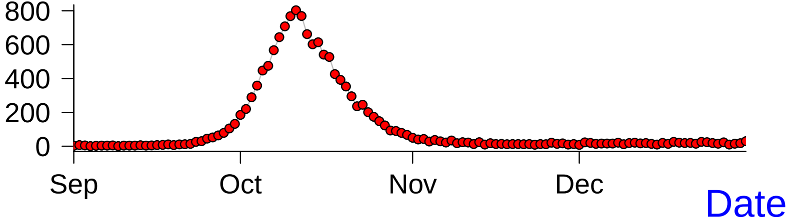
https://surveys.mcmaster.ca/limesurvey/index.php/893454

> *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)*

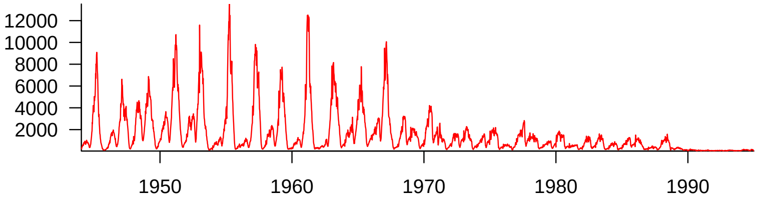
# Epidemic Data Analysis

# Time Plots of Temporal Epidemic Patterns

1918 P&I

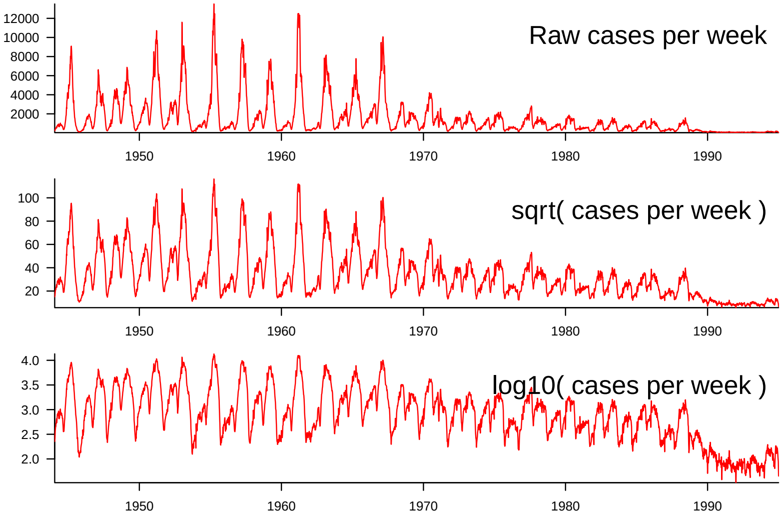



Weekly Measles in England and Wales



# Time Plots of Transformed Data

- Reveal unobvious aspects of time series



# Times Plots of Smoothed Data

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

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

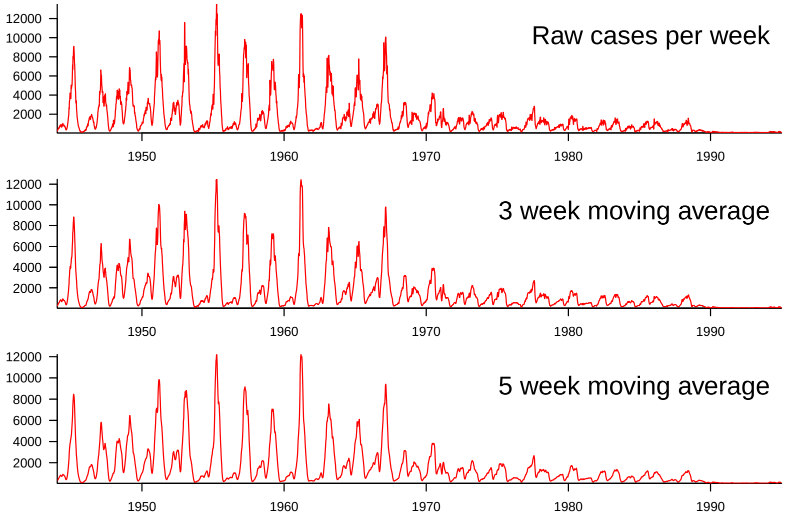
  - Replace original data points $x_t$ with averages of nearby points.

- *Linear filter:*

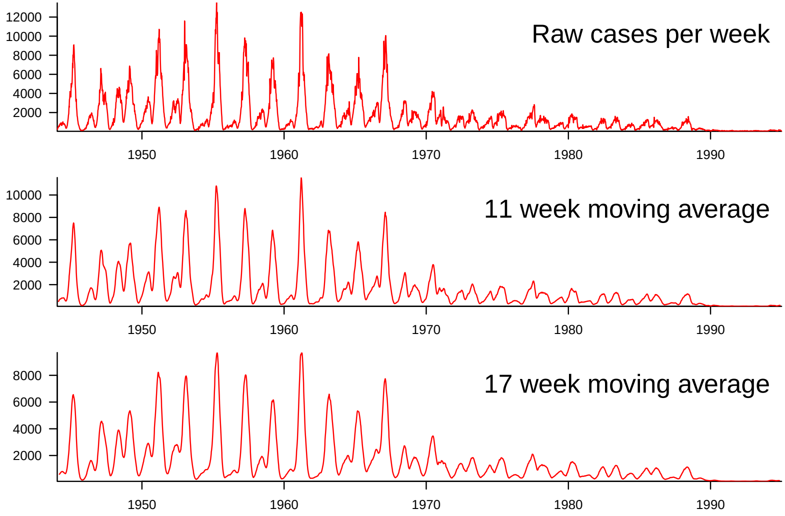
$$x_t \to \sum_{i=-\infty}^{\infty} \lambda_i x_{t+i}$$

  - Generalization of moving average.
  - *Weights* $\lambda_i$ can be nonlinear functions of $i$.

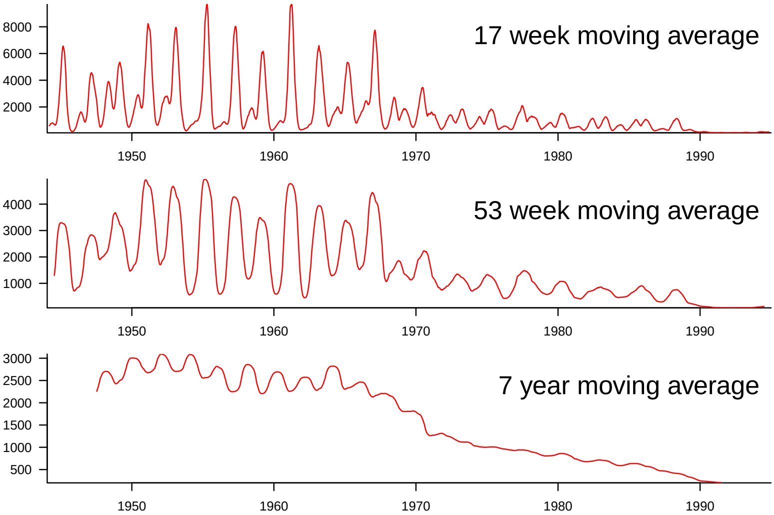
# Times Plots of Smoothed Data



# Times Plots of Smoothed Data



# Times Plots of Smoothed Data



# Correlation

- Recurrent epidemics $\implies$ number of cases now is correlated with number of cases in the past and the future.

- Given $N$ pairs of observations of different quantities, $\{(x_i, y_i) : i = 1, \ldots, N\}$, 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)
- $r = 1 \iff$ 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:* $r^2$ 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

# Autocorrelation

- Given a single sequence of observations $\{x_t : t = 1, \ldots, N\}$, we can compute the correlation of each observation with the observation $k$ time steps in the future.

- Thus, we consider the pairs of observations $\{(x_t, x_{k+t}) : t = 1, \ldots, N-k\}$ 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.

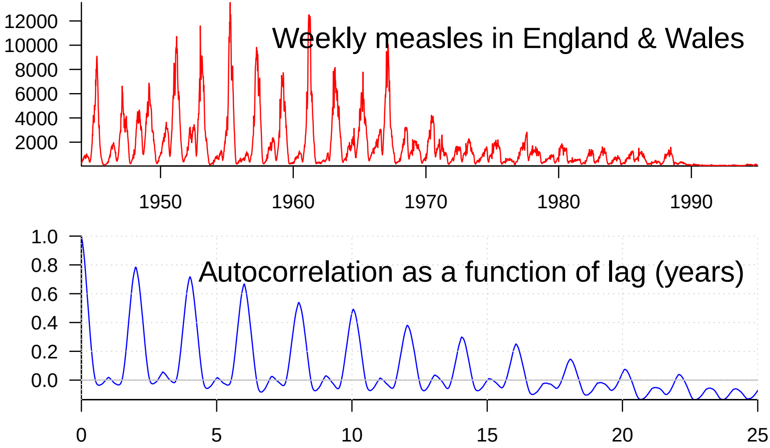
# Autocorrelation

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

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

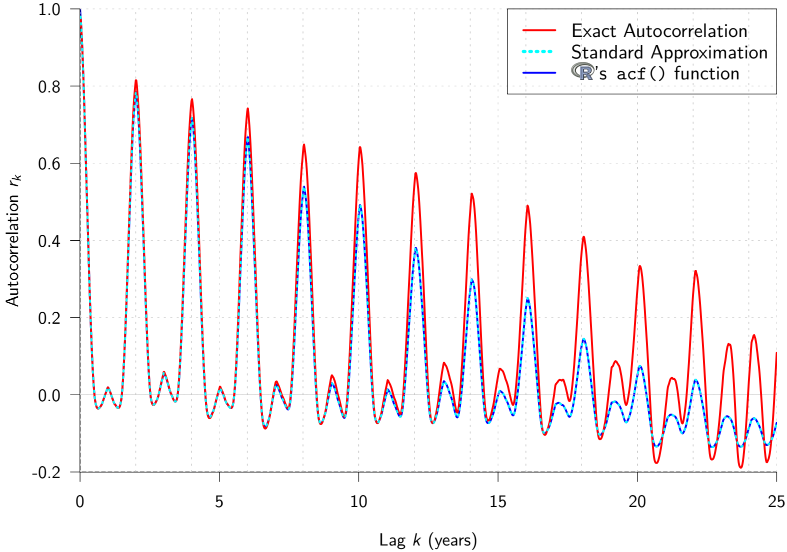
- Approximation of $r_k$ is worse for larger lags $k$
- Plot of autocorrelation $r_k$ as a function of lag $k$ is called the *correlogram*.

# Correlogram




- Peaks in correlogram $\Longrightarrow$ periodicities in original time series.
- Correlograms of temporal segments are often informative.

# Correlogram: exact vs. approximate $r_k$



# Spectral Density

- 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 $\cos \omega_p t$ and $\sin \omega_p t$.

# Spectral Density

- 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 $\omega_p$ is$^\star$:

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

$^\star$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.

# Please consider. . .

**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)*

# Spectral Density

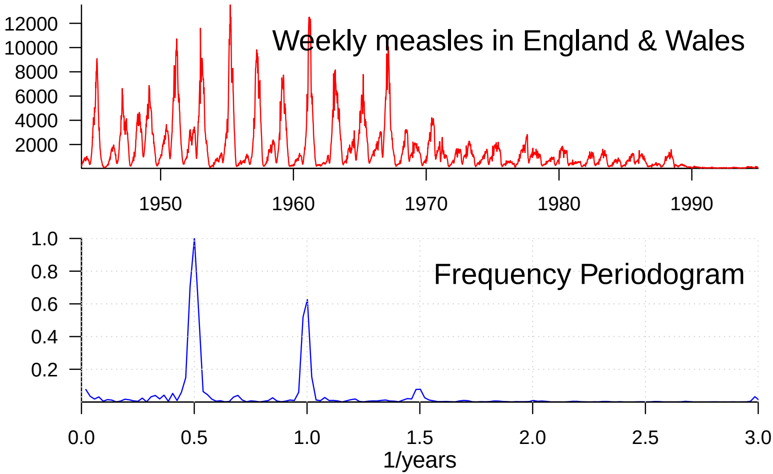
- There are many different ways to express the power spectral density (aka *power spectrum*).

- Most common/useful equivalence is that the power spectrum is the discrete Fourier transform of the correlogram:

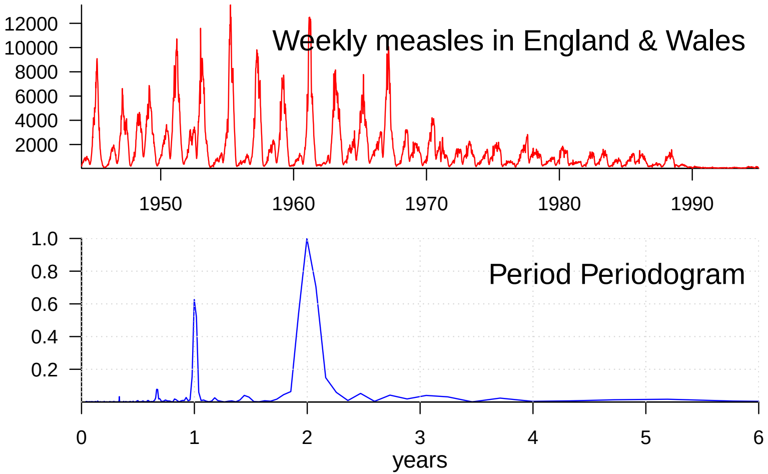
$$I(\omega_p) = \frac{1}{\pi}\left(r_0 + 2\sum_{k=1}^{N-1} r_k \cos\omega_p k\right)$$

- Plot of estimated power spectrum as a function of frequency $\omega_p$ is called the *frequency periodogram* or just the *periodogram*.

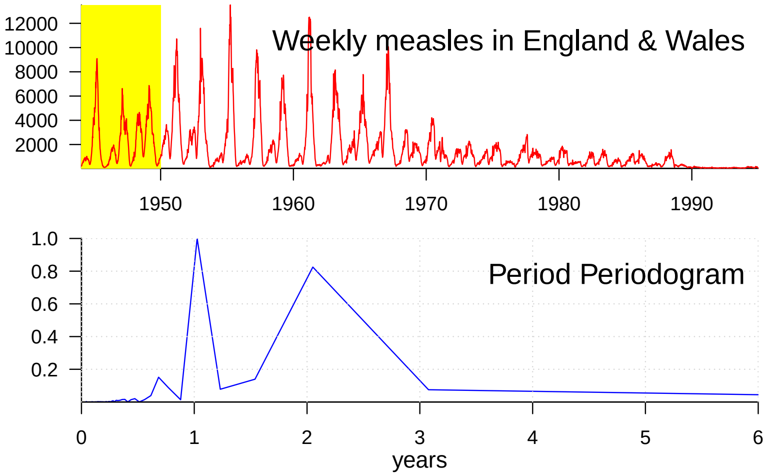
# Spectral Density



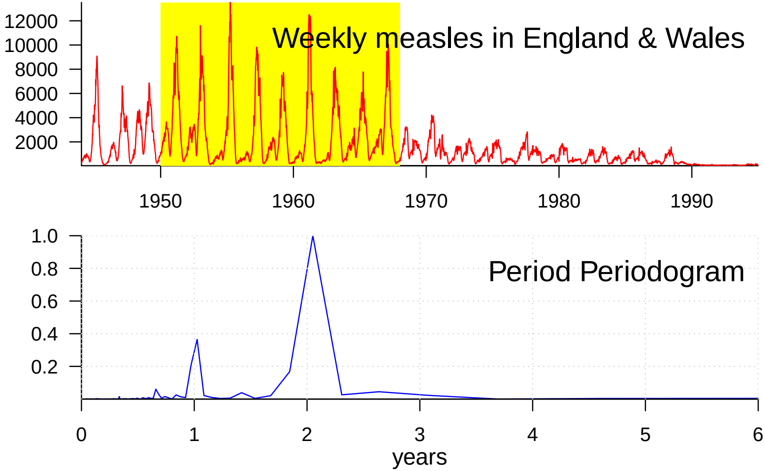
# Spectral Density



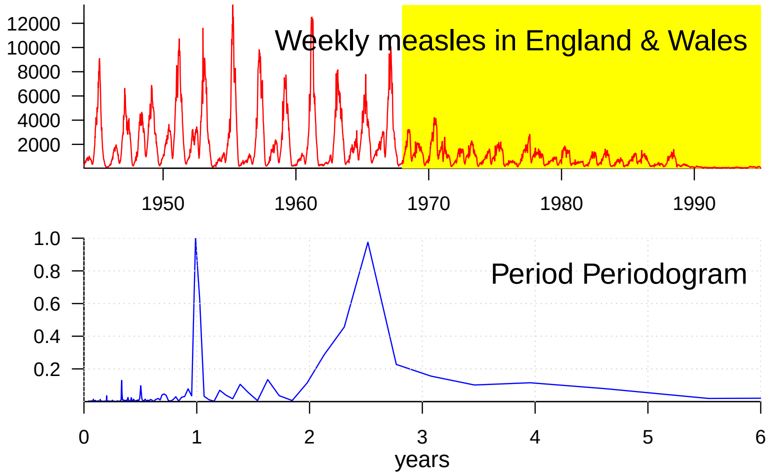
# Spectral Density of Temporal Segments



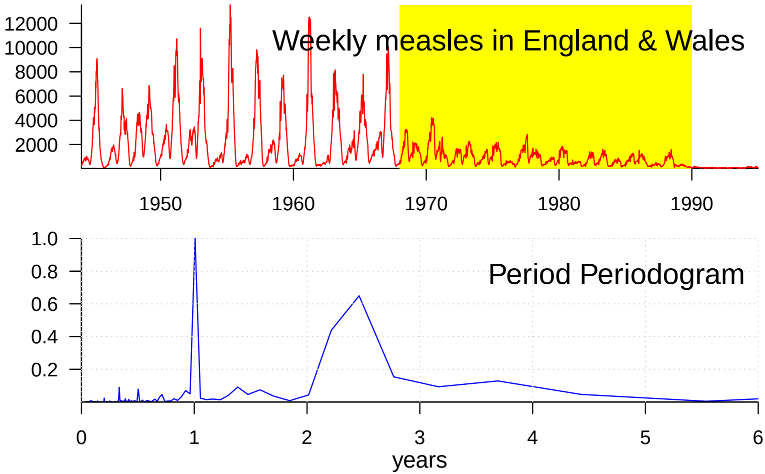
# Spectral Density of Temporal Segments



# Spectral Density of Temporal Segments



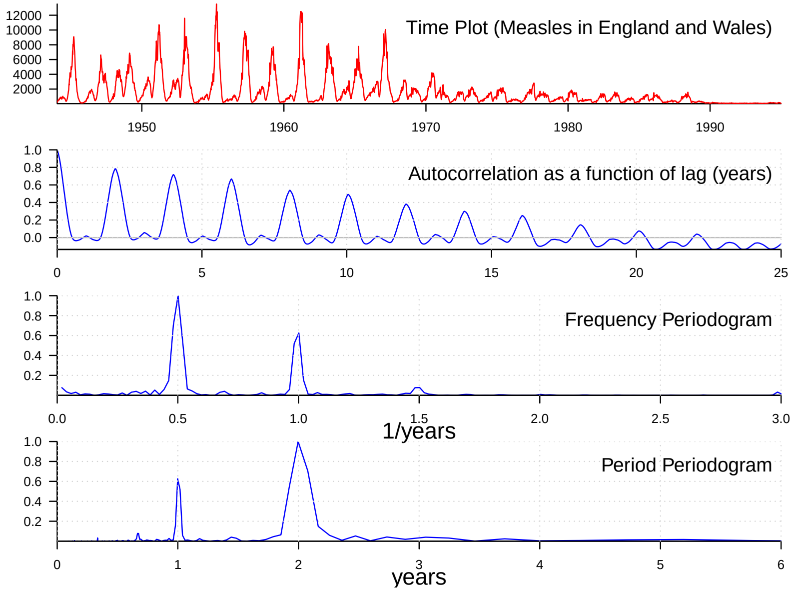
# Spectral Density of Temporal Segments



# Spectral Density Properties

- Periodogram is discrete Fourier transform of correlogram
- Same information in correlogram and periodogram
- Periodogram usually easier to interpret
- In R, calculate power spectrum with `spectrum()`
- The power spectrum $I(\omega_p)$ partitions the variance in the time series with respect to frequency $\omega_p$.
  - 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 $\frac{1}{N}\sum_t (x_t - \bar{x})^2 = \mathrm{Var}\{x_t\}$, 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



McMaster University

Mathematics and Statistics

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

# Mathematics 4MB3/6MB3
# Mathematical Biology

Instructor: David Earn

Lecture 4
Epidemic Data Tools
Monday 30 Sep 2019

# 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

# Attendance

Who is here?

# Spectral Density of Temporal Segments

- Pre-war measles
- Post-war pre-vaccination measles
- Vaccination era measles
- Vaccination era measles until 1990

# Time series analysis functions

R has built-in tools for time series analysis:

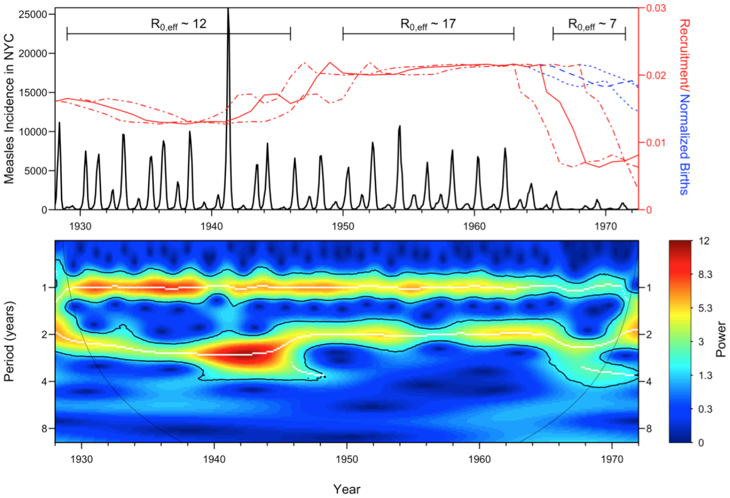
- Time plot: `plot()` *etc.*
- Linear filter (*e.g.*, moving average): `filter()`
- Correlogram (auto-correlation function): `acf()`
- Periodogram (power spectrum): `spectrum()`

You will use all of these functions in **Assignment 4.**

# More sophisticated spectral method

- Traditional power spectrum measures frequency content of entire time series.
- Wavelet decomposition is local in time.
  - Reveals changes in the spectrum over time without having to identify distinct temporal segments yourself.
  - Nice intro to wavelet analysis of time series:
    Torrence and Compo (1998) "A Practical Guide to Wavelet Analysis" *Bulletin of the American Meteorological Society* **79**, 61–78
  - $\exists$ R packages for wavelet analysis of time series (*e.g.*, WaveletComp, wavelets), and at least one book on wavelet methods in R

# Wavelet Spectrum of Monthly Measles in New York City




Krylova & Earn 2013, *J. R. Soc. Interface* **10**, 20130098

# Wavelet Spectrum of Weekly Measles in New York City

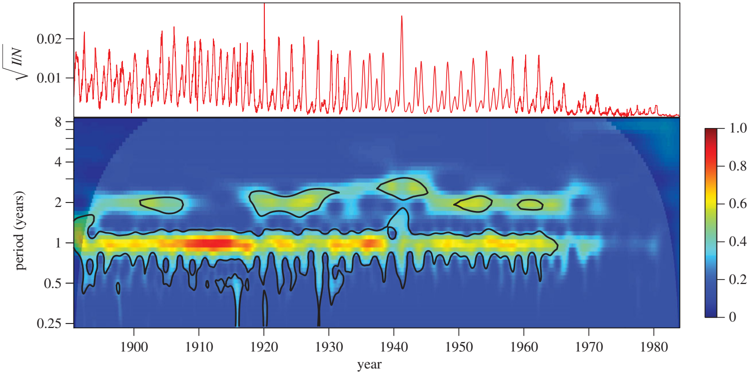
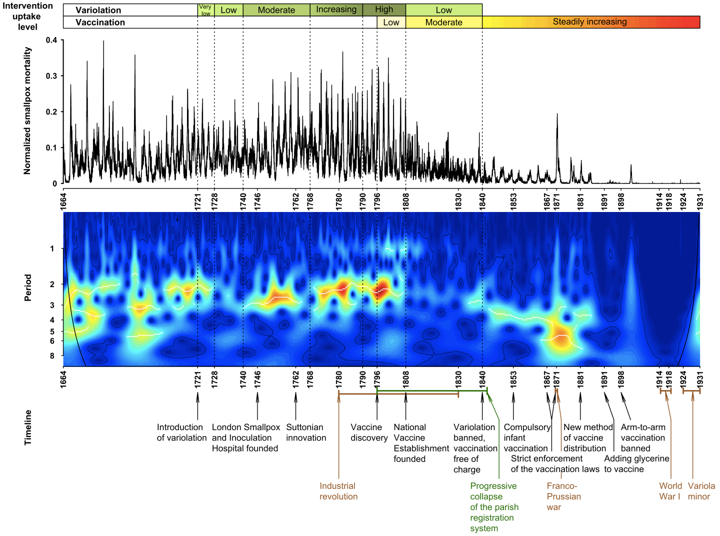



**Figure 5.** Observed measles dynamics in NYC from 1891 to 1984. (*a*) Square root of measles case reports, normalized by total concurrent population. (*b*) Colour depth plot of a continuous wavelet transform of the square root of normalized observed NYC measles cases (colour warmth scales with spectral power and 95% significance contours are shown in black). Shaded regions in the upper left and right indicate the cone of influence.

Hempel & Earn 2015, *J. R. Soc. Interface* **12**, 20150024

# Wavelet Spectrum of Weekly Smallpox in London




Krylova & Earn 2019, *bioRxiv* **doi:** https://doi.org/10.1101/771220

# Statistical Modelling of Time Series

# Statistical Modelling of Time Series

- Imagine time series $\{X_t\}$ is generated by random processes.
- Simplest case: $X_t$ (number of cases at time $t$) is simply a random variable with a known distribution,

$$X_t = \mu + Z_t \qquad (*)$$

  where $\mu =$ time average number of cases
  and $\{Z_t\} =$ sequence of random variables with zero mean.
- Might be a reasonable model for importation of new, infectious individuals into a focal community.
- Bad model for epidemics: ignores transmission from one individual to another.
  - There must be a correlation between the number of individuals in the focal community who are infected now and the number who will be infected in the near future.

# Statistical Modelling of Time Series: AR and MA

- So, imagine that that successive data points in $\{X_t\}$ are correlated.
- For example, perhaps the data are generated by an *autoregressive (AR) process*:

$$X_t - \mu = \alpha_1(X_{t-1} - \mu) + \alpha_2(X_{t-2} - \mu) + \cdots + \alpha_p(X_{t-p} - \mu) + Z_t \,,$$

  where the $\alpha_i$ are constants that determine the degree of correlation along the time series.
- Alternatively, the data might be generated by a *moving average (MA) process*:

$$X_t - \mu = \beta_0 Z_t + \beta_1 Z_{t-1} + \cdots + \beta_q Z_{t-q} \,,$$

  where the $\beta_i$ are constants that define a weighted average.

# Statistical Modelling of Time Series: ARMA

- More generally, the data might be generated by an *autoregressive moving average "ARMA(p, q)" process*:

$$\begin{aligned} X_t - \mu = {} & \alpha_1(X_{t-1} - \mu) + \alpha_2(X_{t-2} - \mu) + \cdots + \alpha_p(X_{t-p} - \mu) \\ & + \beta_0 Z_t + \beta_1 Z_{t-1} + \cdots + \beta_q Z_{t-q} \,. \end{aligned}$$

# Statistical Modelling of Time Series: ARIMA

- Finally, an *autoregressive integrated moving average "ARIMA($p, d, q$)" model* includes weighted differences of the time series:

$$\begin{aligned} X_t - \mu = {} & \alpha_1(X_{t-1} - \mu) + \alpha_2(X_{t-2} - \mu) + \cdots + \alpha_p(X_{t-p} - \mu) \\ & + \gamma_1(X_{t-1} - X_{t-2}) + \gamma_2(X_{t-2} - X_{t-3}) + \cdots \\ & + \beta_0 Z_t + \beta_1 Z_{t-1} + \cdots + \beta_q Z_{t-q} \,. \end{aligned}$$

  - The "I" in ARIMA refers to the original time series $X_t$, which is an "integrated" version of the differenced time series.
  - Technically, an ARIMA model is just an ARMA model with differently labelled coefficients, but explicit differences are often helpful conceptually (*e.g.*, they can "stationarize" a time series).

# What kind of process generated our data?

- *How can we tell if our data were generated by such a process? Can we identify an* $AR(p)$, $MA(q)$ *or* $ARMA(p, q)$ *process?*

- Compare time plots of these processes with time plot of our data? (Comparison by eye often challenging/unreliable.)
- Compare autocorrelation functions (correlograms) of these processes with correlogram of our data? (Better.)
- Compare power spectra (periodograms) of these processes with periodogram of our data? (Even better.)
- Compare wavelet spectra of these processes with wavelet spectrum of our data? (Better yet.)

# Statistical Modelling of Time Series: ARMA fitting

- Looking at the power spectra of ARMA models would be instructive.
- But is there a better approach to discovering if an ARMA model could explain our data?
- Find the *best fit* ARMA parameters by minimizing the residual sum of squares. *e.g.*, for an AR model, minimize:

$$S = \sum_{t=p+1}^{N} \big[(x_t - \mu) - \alpha_1(x_{t-1} - \mu) - \cdots - \alpha_p(x_{t-p} - \mu)\big]^2 .$$

- More generally, we can find the best fit parameters of an ARIMA$(p, d, q)$ model
  - Non-trivial, but there are standard methods
- Compare models with Akaike Information Criterion (AIC), which penalizes models that have more parameters
  - See Earn (2009) review article for more discussion of this.

# Time series tools discussed so far. . .

- Statistical description of time series:
  time plot, moving average, correlation coefficient, autocorrelation, correlogram, power spectral density (PSD), periodogram, wavelet spectrum
- Time series models:
  AR, MA, ARMA, ARIMA

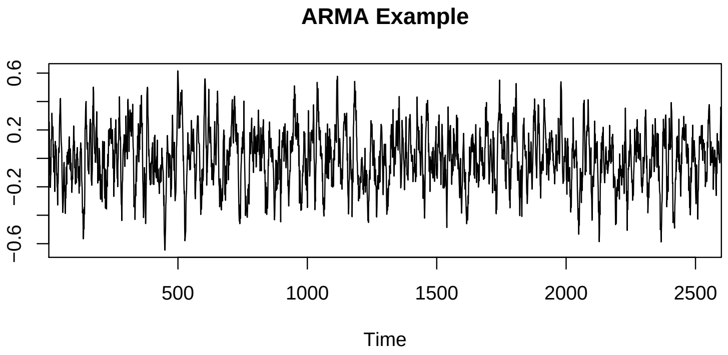
# Statistical Modelling of Time Series

## How to do it in R ...

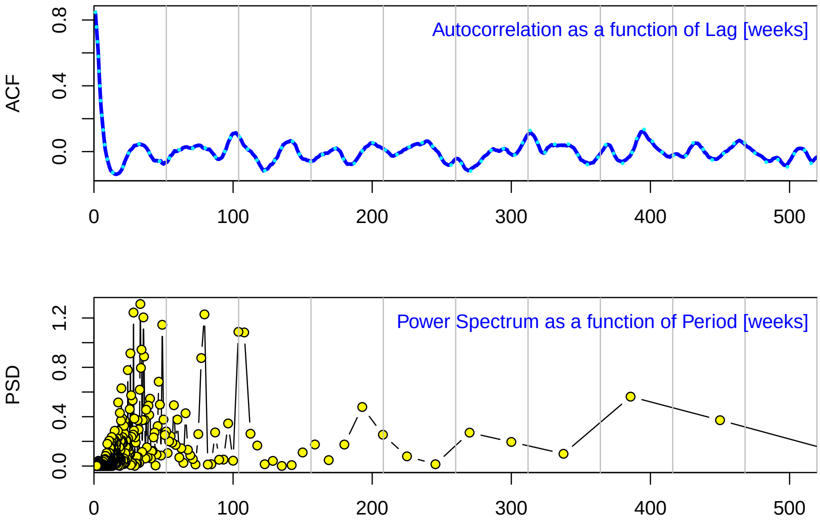
- Simulate any ARIMA($p, d, q$) model with `arima.sim()`
- Fit an AR model to a time series with `ar()`
- Fit an ARIMA model to a time series with `arima()`
- Alternatively, there are specialized time series modelling packages.

# ARMA Example (50 years of weekly data)

```
my.model <- list(ar=c(1,-0.5,0.5,-0.25),ma=c(-0.25,0.5))
my.sim <- arima.sim(n=52*50,model=my.model,sd=0.1)
plot(my.sim,main="ARMA Example",ylab="",xaxs="i")
```



# ARMA Example (ACF and PSD up to 10 year lag)



# Statistical Modelling of Time Series: Forecasting

- Once we have a fitted model, we can then use it to *forecast* future observations
- *Validate* this procedure by using part of the data to fit the model and then forecast the remainder of the data (*cf.* cross-validation)

- How successful is this likely to be for an infectious disease time series?
  - Conceivably good for chicken pox in NYC.
  - Less likely to be good for measles... at least for the main patterns...
  - One of the project options is to look at this more carefully.

# Statistical Modelling of Time Series: Limitations

- It might be best to remove mean, trend and seasonality before fitting an ARMA model
  - But this means we will remove the aspects of the data about which we care most!
- The fitted parameters of an ARMA model have no obvious biological meaning
  - The model completely ignores any understanding we have of infectious disease transmission
- Statistical models use the time series itself to parameterize an ARMA (or more general) process
  - It would be better to have a model that we can parameterize from independently collected data and then see if that model can explain the observed time series

# Mechanistic Mathematical Modelling

- SIR and all that...
- Takes into account transmission process...

- So why did we just spend time talking about statistical modelling?
  - Important to be familiar with time series models that are in common use.
  - Helps us appreciate the value of mechanistic modelling.
  - Some processes that affect disease dynamics might be better modelled as ARMA or similar processes.
    - Weather (*e.g.*, perhaps model $\beta = \beta(t)$ as an ARMA process)
    - Immigration
  - Ruling out an ARMA model (or at least one with a modest number of parameters) is a step towards finding a good model.
  - A combination of mechanistic and time series models could be useful.

# THINKING ABOUT GRADUATE SCHOOL?

JOIN US TO FIND OUT MORE AT THE GRAD INFO SESSION!

**WHEN**: THURSDAY OCTOBER 3, 2019
**TIME**: 5:30PM – 7:00PM
**WHERE**: HH/305 AND THE MATH CAFÉ

Matheus Grasselli will give general advice on applying to grad school.

Shui Feng will talk about graduate programs particular to statistics.

Tom Hurd will talk about graduate opportunities in financial math including PhiMac.

Miroslav Lovric will give tips about applying to teachers' college.

**PIZZA** will be served! See you there!