ICTP January 2015

Lecture

Seasonality and Diseases

Giulio De Leo

Deterministic, autonomous models

Let's consider a typical SIR model:

$$\frac{dS}{dt} = \mu - \beta SI - \mu S$$
$$\frac{dI}{dt} = \beta SI - (\gamma + \mu) I$$
$$\frac{dR}{dt} = \gamma I - \mu R$$

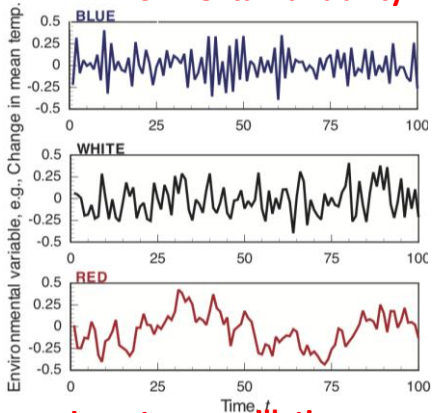
- S, I, R represent the state of the system at time t;
  Note that here the rates of change in time dx_i/dt
  do not depend *explicitly* upon time t (the independent variable).

- μ, β and γ are model parameters (they determine the actual rate at which processes occurs).
  In basic SIR models, they are generally assumed
  to be constant, i.e. they do not change with time.
  These systems are called autonomous or time invariant systems.

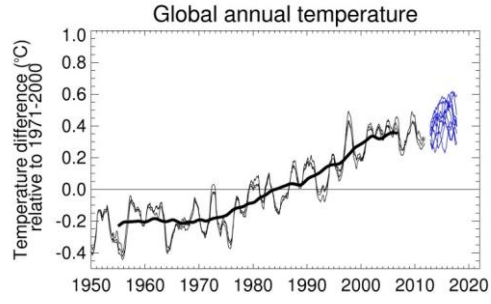
Assumption of time invariance for model parameters might not hold true

- Environmental stochasticity
  - Non deterministic, year-to-year or within year random fluctuations. Modeled through probability distribution functions
- Climate change
  - Long term trends in mean, variance and other statistical properties of meteo-climatic variables, such as temperature, precipitation, humidity, etc.
- Seasonality
  - Periodic, repetitive, and generally regular and predictable pattern typically occurring every calendar year
- Cyclical effects
  - Periodic, repetitive, and more or less regular patterns spanning time periods longer than one calendar year (and potentially over several years or even decades, e.g. El Niño, la La Niña, Pacific Decadal oscillation, interdecadal Pacific oscillation, etc.)

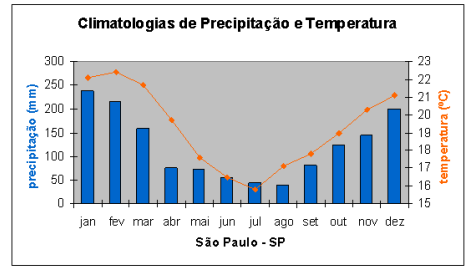
Environmental variability



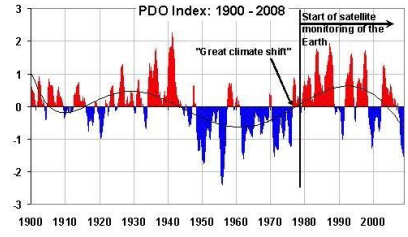
Climate change



Seasonality



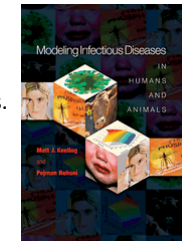
Long term oscillations



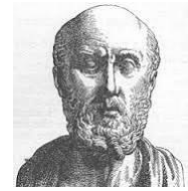
Questions about seasonality

- What is the evidence of seasonal variations in diseases incidence?
- What are the drivers of seasonality?
- How do we incorporate seasonality in our models?
- What is the effect of seasonality on the dynamics of infectious diseases?
- Does the shape of seasonality matters?
- What are the implication for disease control and eradication?

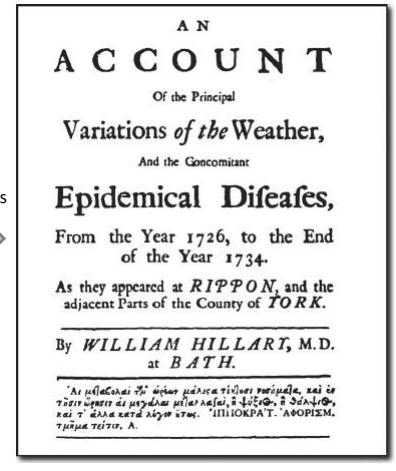
- Main references on seasonality and diseases:
  - Keeling & Rohani 2008. Chapter 5. Princeton University Press.
  - Altizer et al. 2006. Ecology Letters 9:476-484
  - Grassly & Fraser 2006. PRSLB, 273:2541-2550



A little bit of history



- Hippocrates, *On Airs, Waters and Places* 380 BC
  - Sargent, II, Frederick (1982), Hippocratic heritage : a history of ideas about weather and human health, New York: Pergamon Press
- Sydenham
  - *Observationes medicae* 1676 and *Epistola responsoria 1670.* commented on seasonal and recurrent epidemics
- Hillary 1740
- Hirsch A. 1885.
  - Commented on the seasonality of measles typhus, typhoid, yellow fever, cholera etc.
- Soper 1929



A N

A C C O U N T

Of the Principal

Variations *of the* Weather,

And the Concomitant

Epidemical Diſeaſes,

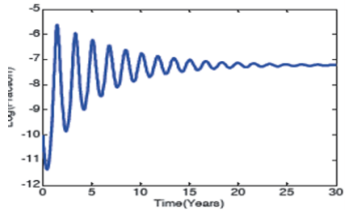
From the Year 1726, to the End of the Year 1734.

As they appeared at *RIPPON*, and the adjacent Parts of the County of *YORK*.

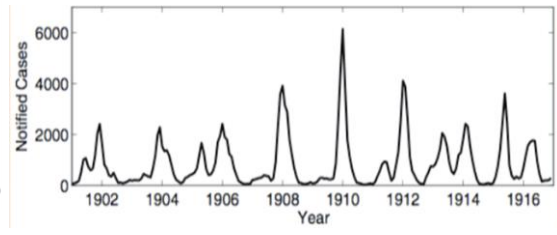
By *WILLIAM HILLARY*, M.D. at *BATH*.

Soper 1929

SI model prediction

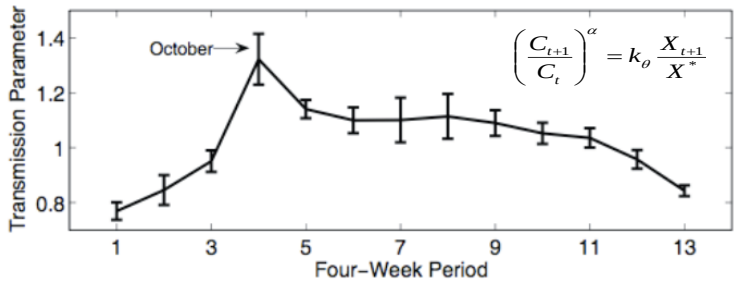


Measles data in Glasgow

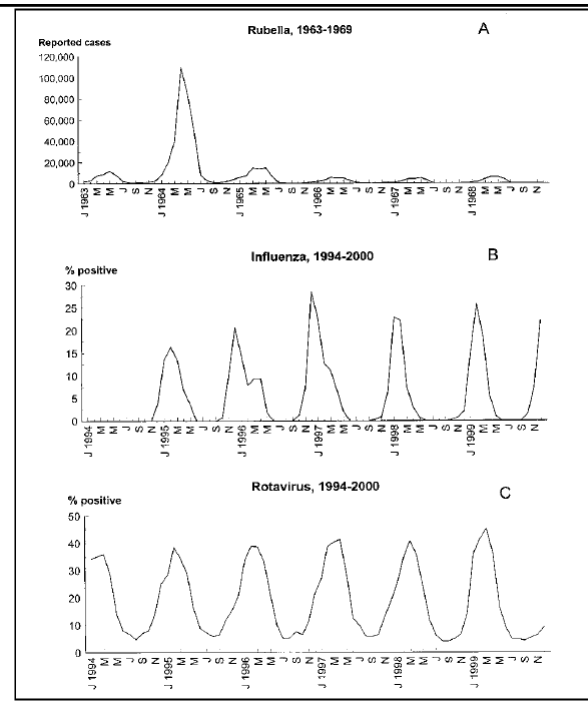


- **Soper wondered why – in direct contrast to predicted damped oscillations from SIR model – wild epidemics were observed**

- Soper suggested that a missing ingredient in basic model was seasonal change, because of "*perturbing influences, such as might be brought about by school break up reassembling, or other annual recurrences*"



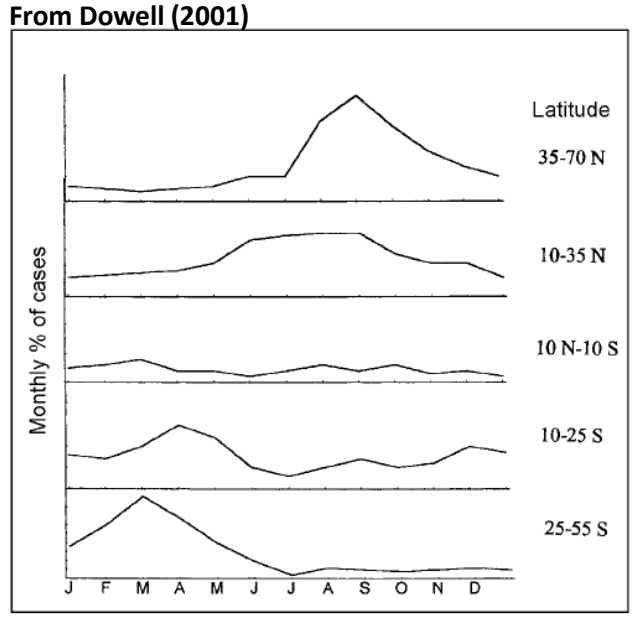
Since then, a large body of work has demonstrated influence of measles, pertussis, chickenpox, rubella and influenza



From Dowell 2001

Seasonal variation in the incidence of poliomyelitis by latitude, 1956-57

From Dowell (2001)

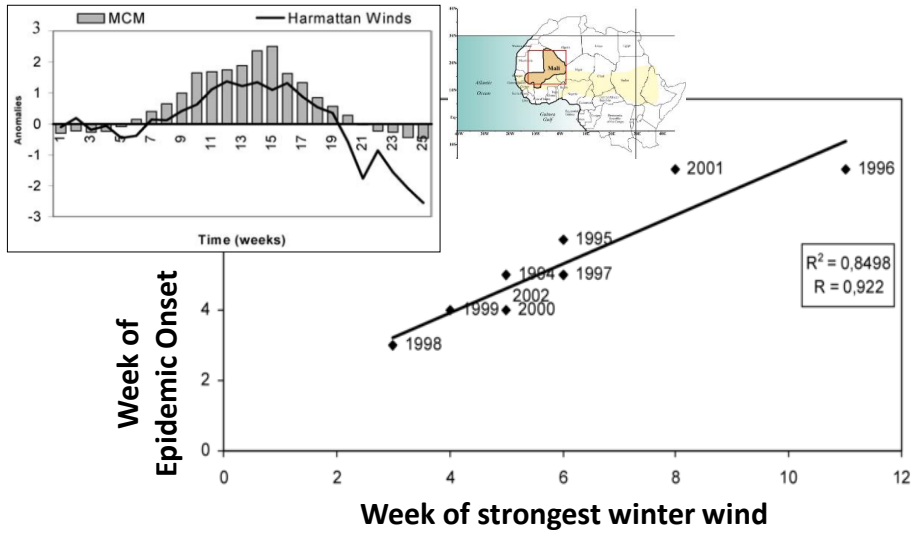


Open access, freely available online PLoS MEDICINE

Climate Drives the Meningitis Epidemics Onset in West Africa

Benjamin Sultan[1*], Karima Labadi[2], Jean-François Guégan[3], Serge Janicot[1]

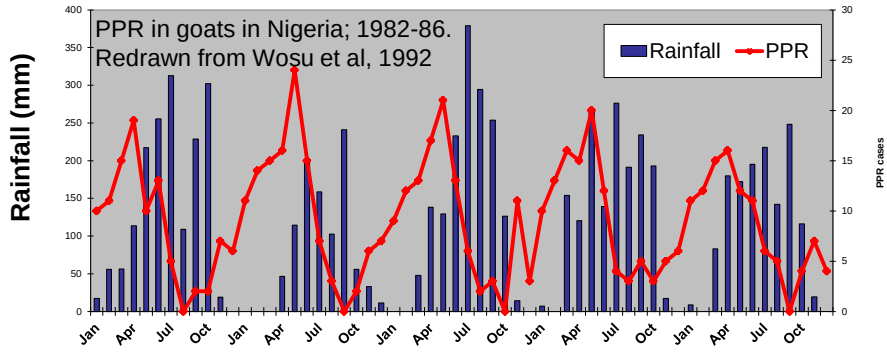
2005



Anecdotic evidence of the link between climatic variability and animal diseases

Peste des petits ruminants

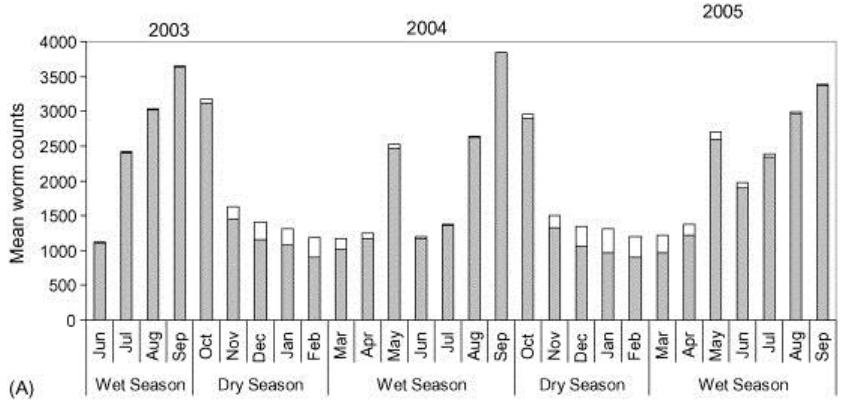
- acute, contagious, viral disease of small ruminants
- transmitted mostly by aerosol droplets between animals in close contact.
- outbreaks associated with the onset of the rainy season or dry cold periods



Available online at www.sciencedirect.com
ScienceDirect
ELSEVIER
veterinary parasitology
Veterinary Parasitology 143 (2007) 311–321
www.elsevier.com/locate/vetpar

Epidemiology and seasonal dynamics of gastrointestinal nematode infections of sheep in a semi-arid region of eastern Ethiopia

Menkir M. Sissay [a,b], Arvid Uggla [a], Peter J. Waller [a,*]



Ecology Letters, (2006) **9**: 467–484 doi: 10.1111/j.1461-0248.2005.00879.x

REVIEWS AND SYNTHESES

Seasonality and the dynamics of infectious diseases

Sonia Altizer,[1]* Andrew Dobson,[2] Parviez Hosseini,[2] Peter Hudson,[3] Mercedes Pascual[4] and Pejman Rohani[1,5]

Abstract

Seasonal variations in temperature, rainfall and resource availability are ubiquitous and can exert strong pressures on population dynamics. Infectious diseases provide some of the best-studied examples of the role of seasonality in shaping population fluctuations. In this paper, we review examples from human and wildlife disease systems to illustrate

Table 1 Parasites and pathogens from humans and vertebrate animals for which seasonal drivers generate annual peaks or longer-term variation in in

Pathogen/disease	Host	Timing of outbreaks	Mechanism of seasonality
Vector-borne diseases			
Malaria (*Plasmodium vivax* and *Plasmodium falciparum*)	Humans	Peak transmission during warm or rainy seasons	Rainfall and temperature affect mosquito vector abundance, biting rates and parasite development within vectors
Dengue haemorrhagic fever (dengue viruses type 1–4)	Humans	Peak case rates during hot-dry and rainy season	Rainfall and temperature affect mosquito vector abundance, temperature influences parasite replication in vectors
West Nile virus	Avian hosts, humans, other vertebrates	Human cases peak in summer and early fall in temperate regions	Temperature and rainfall affect mosquito vector abundance; temperature influences parasite replication in vectors
Tick-borne encephalitis virus	Rodents, humans	Transmission during spring and summer; persistence depends on seasonality	Virus occurs in areas with seasonal synchrony of larval and nymph ticks as determined by rapid fall cooling
Diarrhoeal diseases			
Cholera (*Vibrio cholerae*)	Humans	One or two annual peaks in spring and fall	Rainfall and temperature influence pathogen survival and transmission
Rotavirus infections	Humans	Winter peaks; timing shifts with latitude	Aggregation of children could elevate contacts and transmission
Respiratory-aerosol and contact-borne pathogens			
Measles (morbillivirus)	Humans	Increases in fall or spring	Host aggregation during school terms increases transmission

- So, there are plenty of seasonal fingerprints in the appearance of recurrent epidemics

Outline

- What is the evidence of seasonal variations in diseases incidence?

→What are the drivers of seasonality?

- How do we incorporate seasonality in our models?
- What is the effect of seasonality on the dynamics of infectious diseases?
- Does the shape of seasonality matters?
- What are the implication for disease control and eradication?

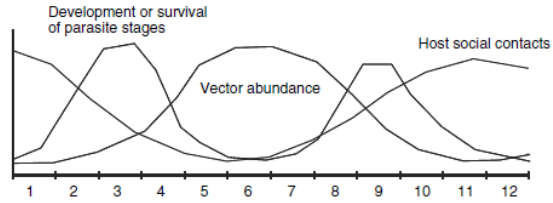
What causes seasonality?

- Host behavior
  - National feasts, public events, and ceremonies
  - School terms
  - Seasonal migration between urban and country sides
  - Wildlife host behavior

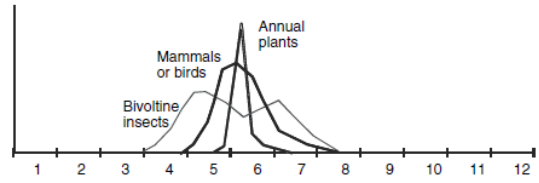
Source: Altizer et al. 2006

Processes important to parasite transmission →

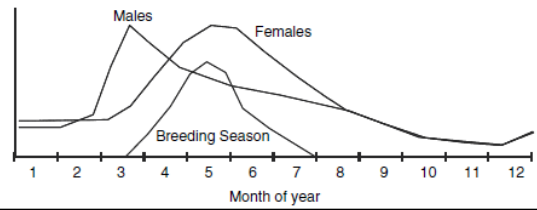
- Effect of seasonal variations of physical parameters (temperature, humidity, rainfall, salinity, flow, etc.)
  - on Vibrio cholera
  - Nematodes' free living stages
  - Vector survival



Host birth rate →



Host susceptibility →



Outline

- What is the evidence of seasonal variations in diseases incidence?
- What are the causes of seasonality?

→ How do we incorporate seasonality in our models?

- What is the effect of seasonality on the dynamics of infectious diseases?
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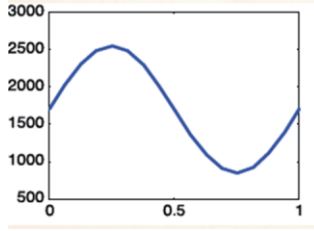
How do we incorporate seasonality? (Part I)

- Let's focus on seasonality in transmission rate β
- We need to make β a function of time β*(t)*



$$\frac{dS}{dt} = \mu - \beta(t)SI - \mu S$$
$$\frac{dI}{dt} = \beta(t)SI - (\gamma + \mu)I$$
$$\frac{dR}{dt} = \gamma I - \mu R$$

$$\beta(t) = \beta_0\left(1 + \beta_1 \cos(\omega t)\right)$$

- β_0: Mean contact rate
- β_1: Amplitude of forcing
- ω: Frequency of forcing

NB: ω = 2π when period of seasonality is 1 yr

Outline

- What is the evidence of seasonal variations in diseases incidence?
- What are the causes of seasonality?
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→What is the effect of seasonality on the dynamics of infectious diseases?

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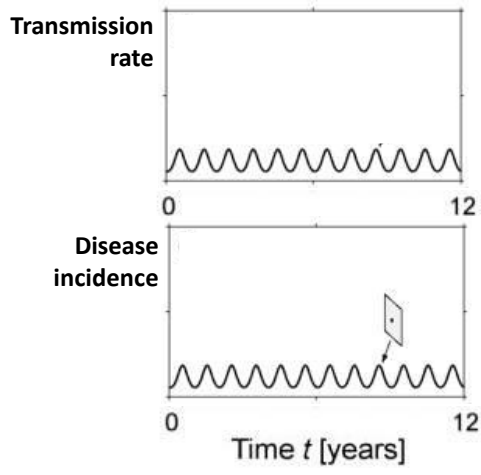
The simplest case:
seasonal fluctuations in transmission rate translate into fluctuations of *similar period and magnitude* in disease incidence

$$\beta(t) = \beta_0(1 + \beta_1 \cos(\omega t))$$



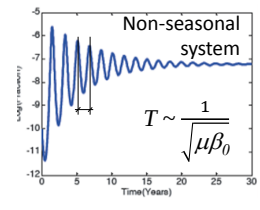
Bailey's (1975) SIR model

$$\frac{dS}{dt} = \mu N - \beta(t) SI / N$$
$$\frac{dI}{dt} = \beta(t) SI / N - \gamma I$$

$$\beta(t) = \beta_0(1 + \beta_1 \cos(\omega t))$$

- Bailey explored the dynamics of small perturbation to the unforced equilibrium assuming a small amplitude of seasonality ($\beta_1 << 1$).
- The magnitude M of the forced system is:

$$M = \frac{2\pi\beta_1\gamma}{\sqrt{\left(\mu\beta_0 - \omega^2\right)^2 + \left(\omega\mu R_0\right)^2}}$$



where:

ω is the frequency of the forcing function

$F = \sqrt{\mu\beta_0}$ the intrinsic frequency of oscillations of the unforced system

By making the appropriate substitutions for measles (K&R page 160-161):

- $1/\gamma$ =13 days
- $\mu = 0.02\ y^{-1}$
- $R_o = 17$

- $\beta_0 = 500$
- $T_{int} = 2\pi/F_{int} = 2.1$ y
- $T_{for} = 2\pi/\omega = 1$ y

$$M = 7.76\beta_1$$

Therefore, a 10% variation in the transmission parameter translates into seasonal variations of 78% in case notification

➔ Relatively modest levels of variation in the transmission rate can translate into large amplitude fluctuations in the observed disease incidence

Moreover…

as $$M = \frac{2\pi\beta_1\gamma}{\sqrt{\left(F^2-\omega^2\right)^2+\left(\omega\mu R_0\right)^2}}$$

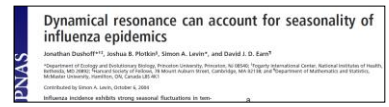
Natural frequency of oscillation

Frequency of oscillation of the forcing function

→ forcing is most greatly amplified when the intrinsic period of oscillation $T_{int}=2\pi/F$ is close to the period of the seasonal forcing function, i.e. 1 year ($F \to \omega$)

Influenza model by Dushoff et al. 2004 PNAS

$$\frac{dS}{dt} = \frac{N-S-I}{L} - \frac{\beta(t)SI}{N}$$
$$\frac{dI}{dt} = \frac{\beta(t)SI}{N} - \frac{I}{D}$$


PNAS

Dynamical resonance can account for seasonality of influenza epidemics

Jonathan Dushoff*†‡, Joshua B. Plotkin§, Simon A. Levin*, and David J. D. Earn¶

*Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08540; †Fogarty International Center, National Institutes of Health, Bethesda, MD 20892; ‡Harvard Society of Fellows, 78 Mount Auburn Street, Cambridge, MA 02138; and ¶Department of Mathematics and Statistics, McMaster University, Hamilton, ON, Canada L8S 4K1

Contributed by Simon A. Levin, October 6, 2003

Influenza incidence exhibits strong seasonal fluctuations in tem-

where:

D = duration on infectiousness (6 – 8 days)

L = duration of immunity (4-8 years)

N = 500,000

$\beta(t) = \beta_0\left(1+\beta_1\cos(\omega t)\right)$

$R_0 = D\beta_0 =$ 10

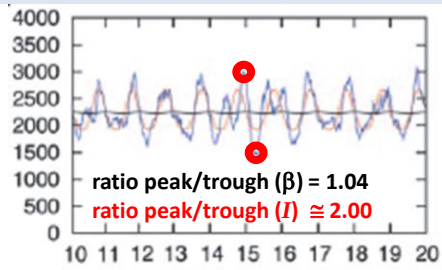
β_1 = 0.04

→ Endogenous period of oscillation: $T = 2\pi\sqrt{DL/(R_0-1)}$

T between 0.4 and 1.5 years

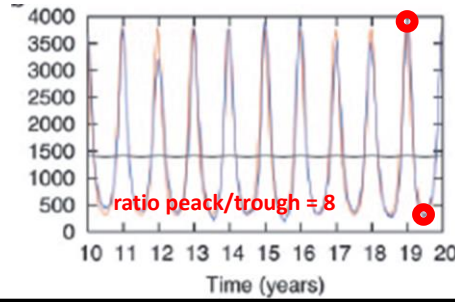
D = duration of infection L = duration of immunity Dushoff et al. 2004 PNAS

D = 0.02 yr L = 4 yr β_o = 500 β_1 = 0.02 → T=0.59 yr



→Harmonic oscillations

D = 0.0025 yr L = 8 yr β_o = 400 β_1 = 0.02 → T=0.94 yr



→ Harmonic resonance

Duration on infection (D)
Duration of immunity (L)
Mean transmission rate (β_0)

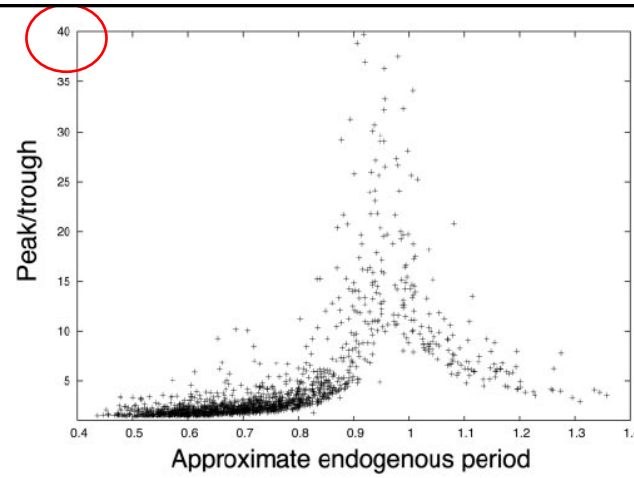


Fig. 2. Magnitude of observed oscillations (ratio of peak-to-trough incidence) in the stochastic forced SIRS epidemic model plotted against the approximated period of endogenous oscillations in the SIRS model $[2\pi\sqrt{DL/(\mathcal{R}_0-1)}]$, for 2,000 sets of parameters randomly chosen from the ranges given in the text (shown are the 1,560 trials where the disease persisted for at least 20 years after being started from the deterministic equilibrium). Underlying variation in transmission rate is ±4% (i.e., β_1 = 0.04 in Eq. 3). Strong resonance occurs when the approximate endogenous period is near 1 year.


Dynamical resonance can account for seasonality of influenza epidemics

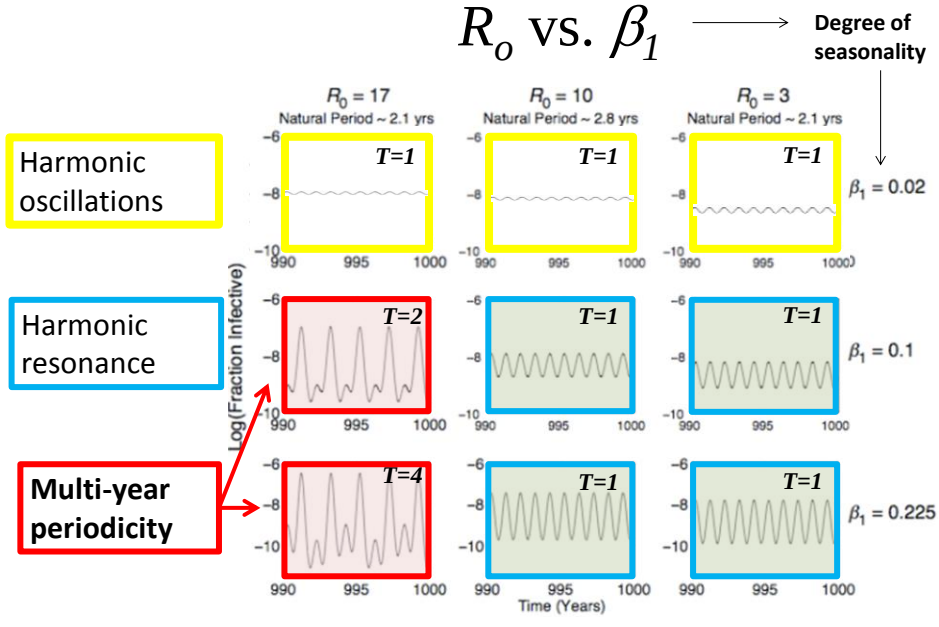
Effect of seasonality

- So, if $F \cong \omega$ → forcing is most greatly amplified, oscillations have same period of the forcing function (i.e. 1 yr)

- What happen if $F < \omega$?
- If the intrinsic period of oscillation is close to an integer multiple of the period of the forcing function, i.e. $\omega/F \cong 2, 3, 4, \ldots, n$

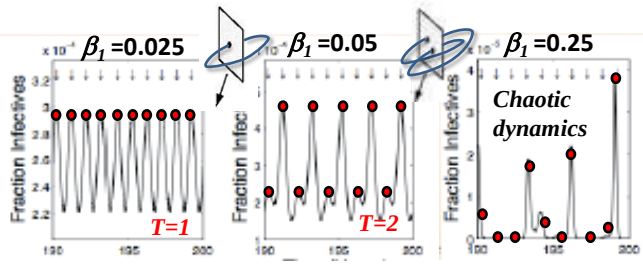
→ then *sub-harmonic resonance*
(multi-years periodicity)

Dietz (1976)

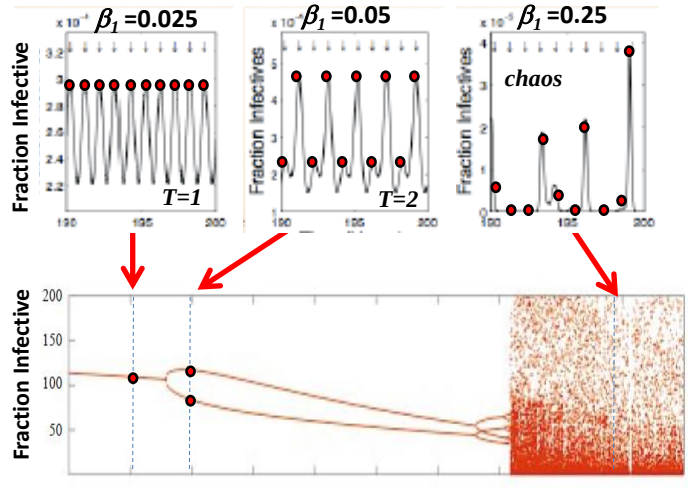


Constructing a bifurcation diagram

- Choose a starting value for control parameter (eg β_1=0.025)
- Set model's initial conditions (eg $S(0) = 0.01$, $I(0) = 0.01$
- Integrate for some period (eg. 200 years)
- For final 10 years of the simulation, note I_ζ at the same time every year (eg October 1st)
- Use a scatter plot to draw I_ζ against value of β_1
- Slightly increase value of control parameter and repeat



A bifurcation diagram



THE ROYAL SOCIETY

Population dynamic interference among childhood diseases

Pejman Rohani*, David J. Earn, Bärbel Finkenstädt and Bryan T. Grenfell
Department of Zoology, University of Cambridge, Downing Street, Cambridge CB2 3EJ, UK

Seasonally forced rabid SEI model

Bolzoni et al. 2008a, Bolzoni et al. 2008b

Susceptibles $dS/dt = aS - (b + \gamma N)S - \beta SI$

Exposed (infected but not yet infective) $dE/dt = \beta SI - (\sigma + b + \gamma N)E$

Infective $dI/dt = \sigma E - (\alpha + b + \gamma N)I$

$N = S + E + I$

a = *fertility rate*
b = *natural mortality*
β = transmission rate
α = *disease-induced mortality*
γ = *density dependence*
σ = *transition rate* $E \rightarrow I$
K = *carrying capacity* $= (a - b)/\gamma$

Nature Vol. 289 26 February 1981 765

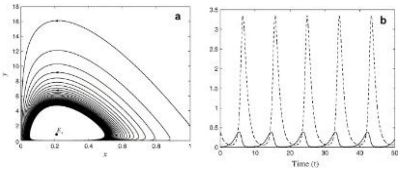
Population dynamics of fox rabies in Europe

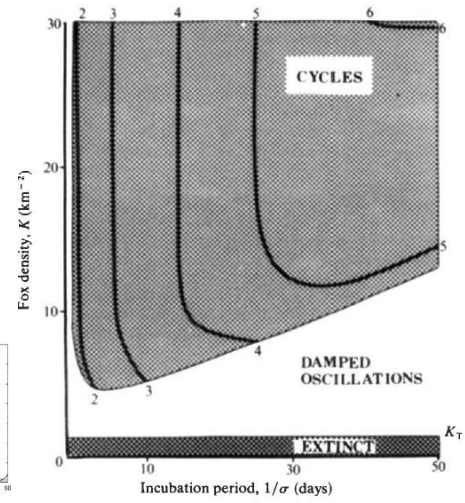
Roy M. Anderson*, Helen C. Jackson†, Robert M. May‡ & Anthony M. Smith*

NB: For suitable combinations of model parameters , i.e.

- high transmission rate β or
- high carrying capacity K
- and long incubation time

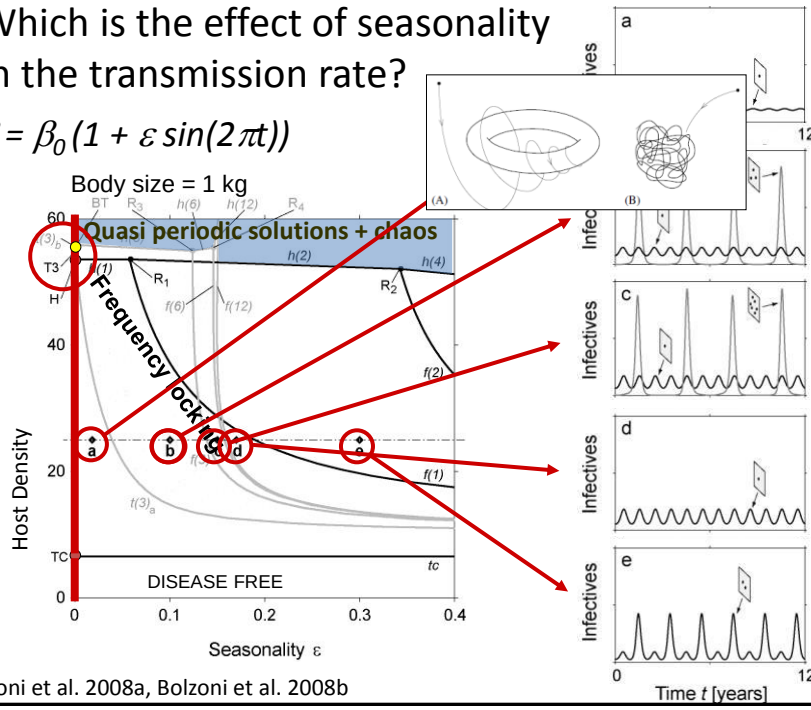
the autonomous (non-seasonal) system exhibits sustained oscillations





Which is the effect of seasonality in the transmission rate?

$\beta = \beta_0 (1 + \varepsilon \sin(2\pi t))$



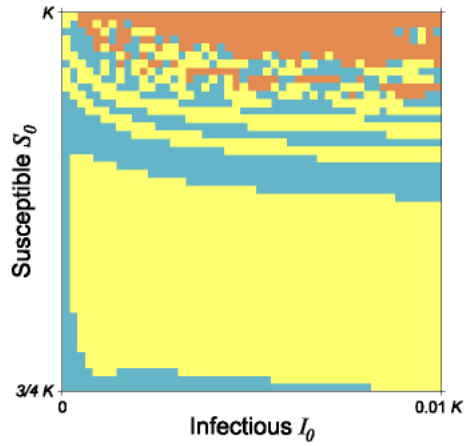
Bolzoni et al. 2008a, Bolzoni et al. 2008b

- In seasonally forced models, more than one possible qualitative dynamical behavior may exist for the same set of model parameters (generally higher values of β_1)

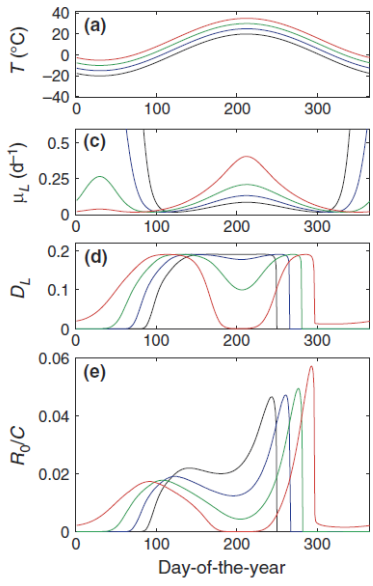
  → there are **multiple stable attractors**

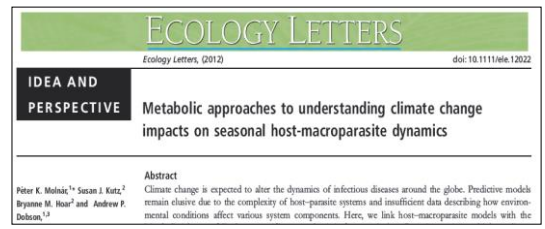
  and which attractor is observed depends upon the initial conditions

Size of the basin on attraction (b) for different initial conditions



If we add environmental noise, there is the possibility of switching from a period-3 cycle to cycles of period 1 or 4 and *vice versa*




ECOLOGY LETTERS

Ecology Letters, (2012) doi: 10.1111/ele.12022

IDEA AND PERSPECTIVE

Metabolic approaches to understanding climate change impacts on seasonal host-macroparasite dynamics

Peter K. Molnár,[1]* Susan J. Kutz,[2] Brynne M. Hoar[2] and Andrew P. Dobson,[1,3]

Abstract

Climate change is expected to alter the dynamics of infectious diseases around the globe. Predictive models remain elusive due to the complexity of host–parasite systems and insufficient data describing how environmental conditions affect various system components. Here, we link host–macroparasite models with the

Outline

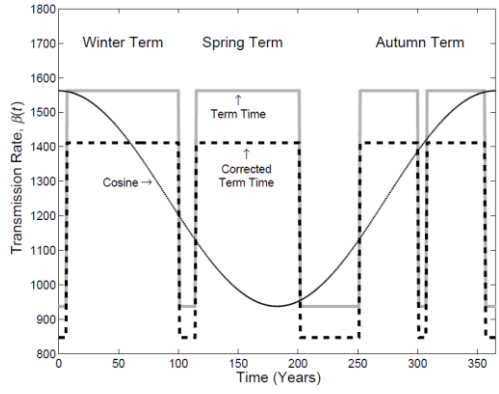
- What is the evidence of seasonal variations in diseases incidence?
- What are the causes of seasonality?
- How do we incorporate seasonality in our models?
- What is the effect of seasonality on the dynamics of infectious diseases?

→ **Does the shape of seasonality matters?**

- What are the implication for disease control and eradication?

Does the shape of the forcing function matter?

- Is seasonality is driven by schools, a "square wave" might be more appropriate

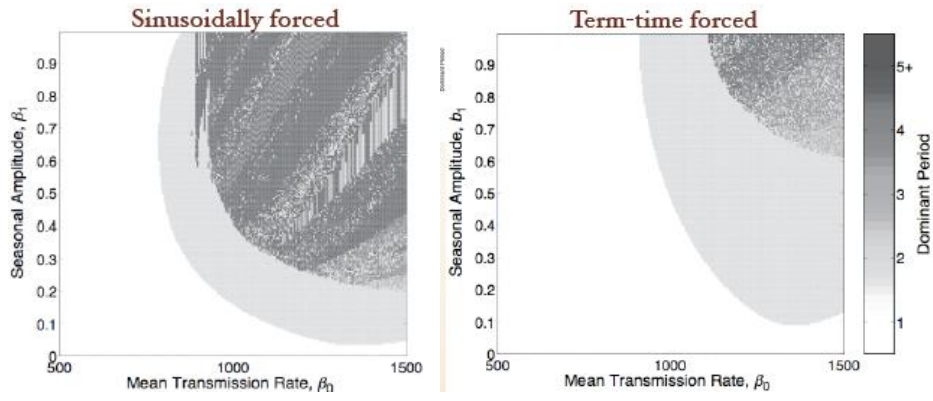


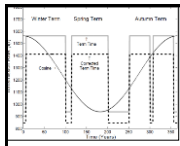
$$\beta(t) = \beta_0\left(1 + \beta_1 term(t)\right)$$

- β_1 is the amplitude of seasonality
- "term(t)" is +1 during school terms and -1 during holiday
- Mean transmission β_0 needs to be tuned by taking into account that there are 92 holidays and 273 school days

Does it matter?

PHYSICA D
Physica D 148 (2001) 317–335
Seasonally forced disease dynamics explored as switching between attractors
Matt J. Keeling*, Pejman Rohani, Bryan T. Grenfell





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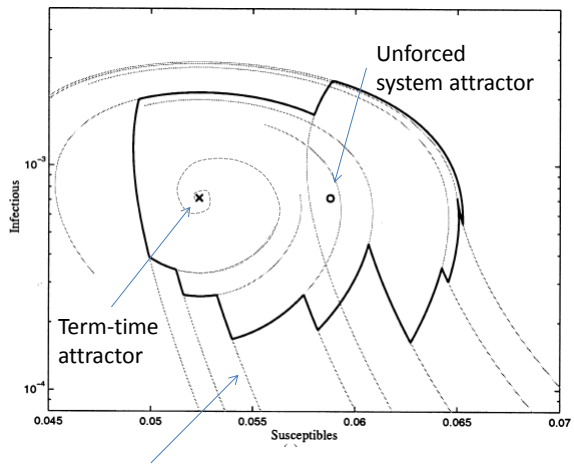
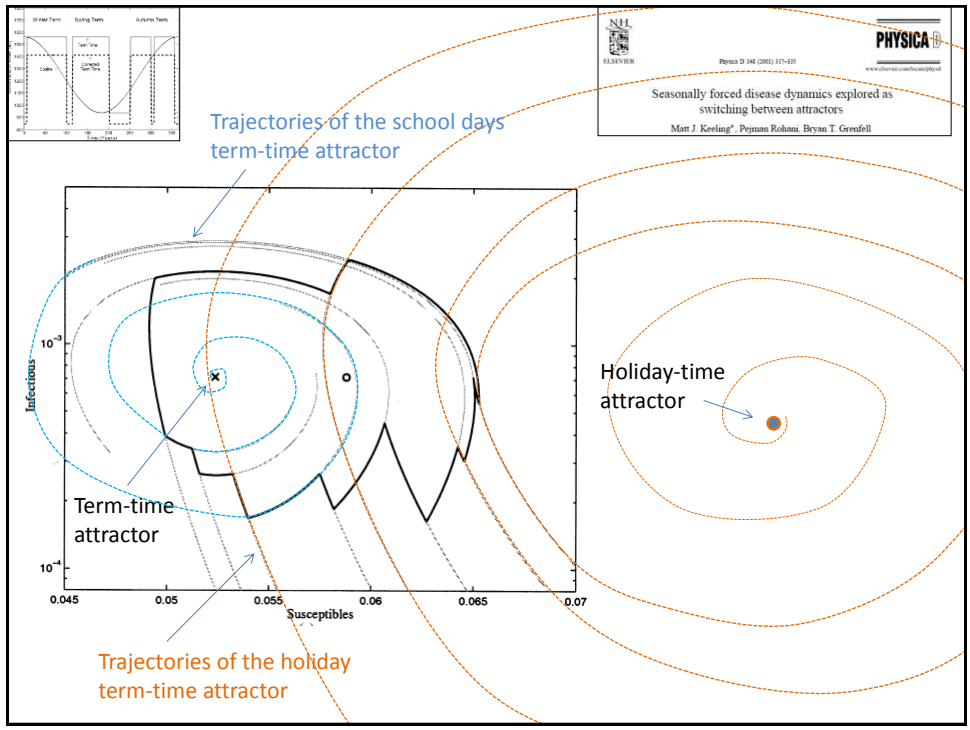
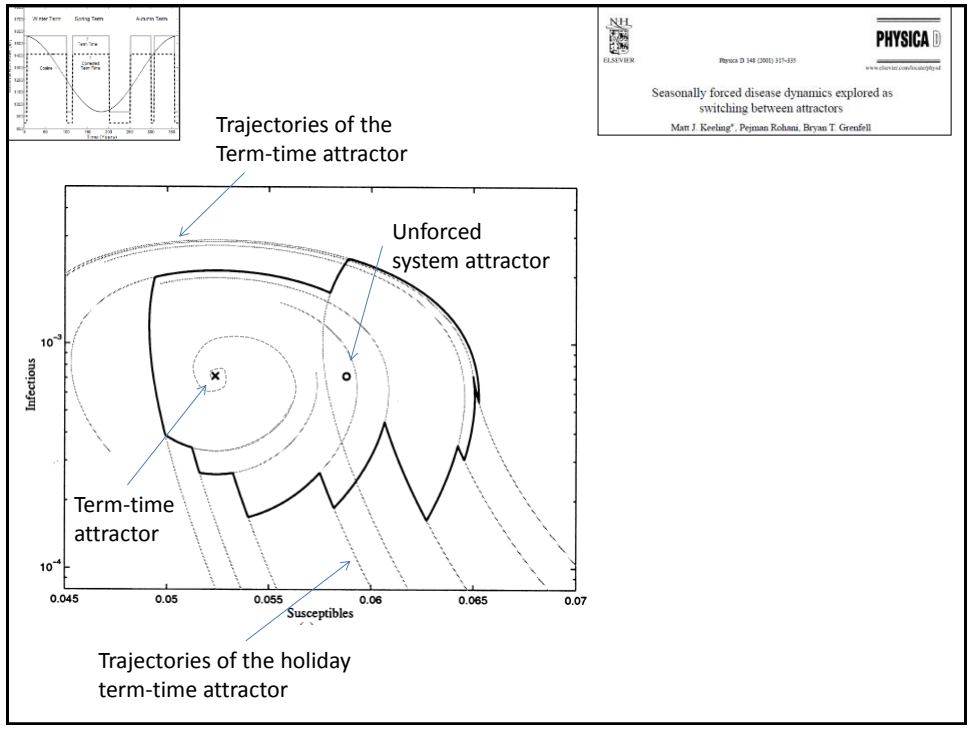



Trajectories of the school days
term-time attractor
Seasonally forced disease dynamics explored as
switching between attractors
Matt J. Keeling*, Pejman Rohani, Bryan T. Grenfell
PHYSICA D
Holiday-time
attractor
Term-time
attractor
Trajectories of the holiday
term-time attractor
Infectious
Susceptibles
0.045
0.05
0.055
0.06
0.065
0.07


Trajectories of the
Term-time attractor
Seasonally forced disease dynamics explored as
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PHYSICA D
Unforced
system attractor
Term-time
attractor
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0.045
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Outline

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- Does the shape of seasonality matters?

→ **What are the implication for disease control and eradication?**

Effect of control

A Simple Model for Complex Dynamical Transitions in Epidemics

David J. D. Earn,[1,2*] Pejman Rohani,[2] Benjamin M. Bolker,[3] Bryan T. Grenfell[2]

- Consider a SIR model with a fraction p of newborns vaccinated

$$\frac{dS}{dt} = \nu(1-p) - \beta(t)SI - \mu S$$
$$\frac{dI}{dt} = \beta(t)SI - (\gamma + \mu)I$$
$$\frac{dR}{dt} = \gamma I - \mu R$$

- Now, let's do a linear change of the state variables of the model

$$S = s(1-p)$$
$$I = i(1-p)$$
$$R = r(1-p) + p\nu/\mu$$

Effect of control

A Simple Model for Complex Dynamical Transitions in Epidemics

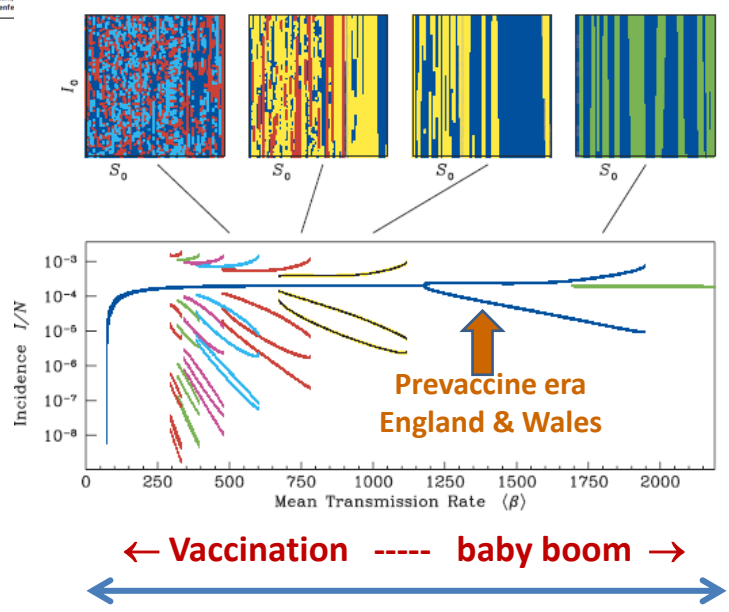
David J. D. Earn,[1,2*] Pejman Rohani,[2] Benjamin M. Bolker,[3] Bryan T. Grenfell[2]

- By substituting into the system, after some simplifications…

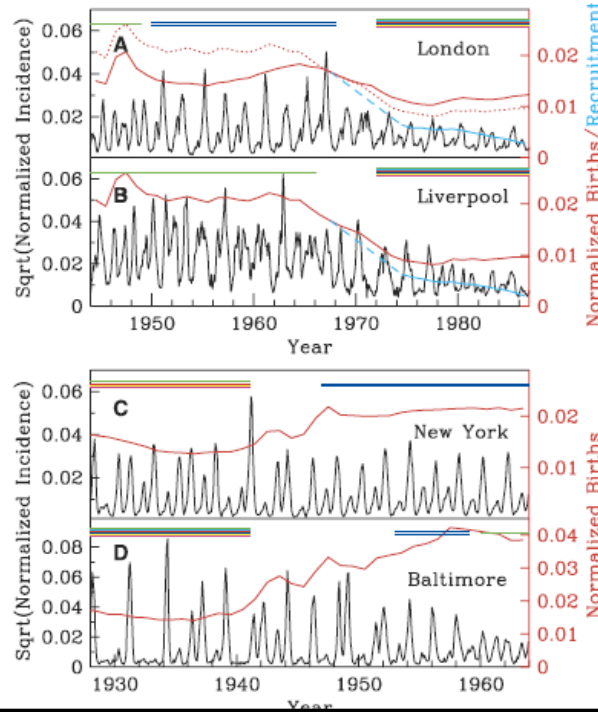
$$\frac{ds}{dt} = \nu - \beta(t)(1-p)si - \mu i$$
$$\frac{di}{dt} = \beta(t)(1-p)si - (\gamma + \mu)i$$
$$\frac{dr}{dt} = \gamma i - \mu r$$

- Therefore, under vaccination, system reduces to basic SIR model with transmission rate β corrected for vaccination effort
- Similarly, if birth rates ν were to change to ν', the transmission rate β would be replaced with βν'/ν

A Simple Model for Complex Dynamical Transitions in Epidemics



← Vaccination ----- baby boom →

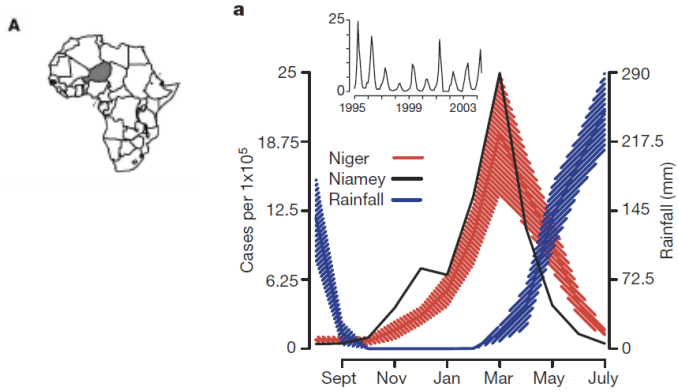


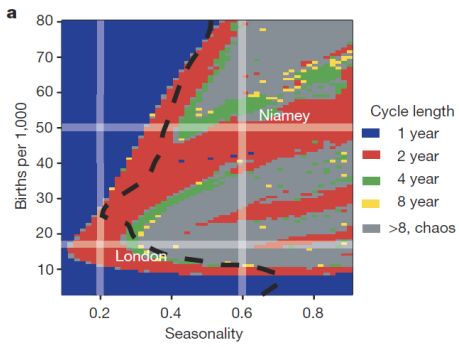
Vol 451|7 February 2008|doi:10.1038/nature06509 nature

ARTICLES

The dynamics of measles in sub-Saharan Africa

Matthew J. Ferrari[1], Rebecca F. Grais[4], Nita Bharti[2], Andrew J. K. Conlan[5], Ottar N. Bjørnstad[1,6], Lara J. Wolfson[7], Philippe J. Guerin[4], Ali Djibo[8] & Bryan T. Grenfell[2,6]





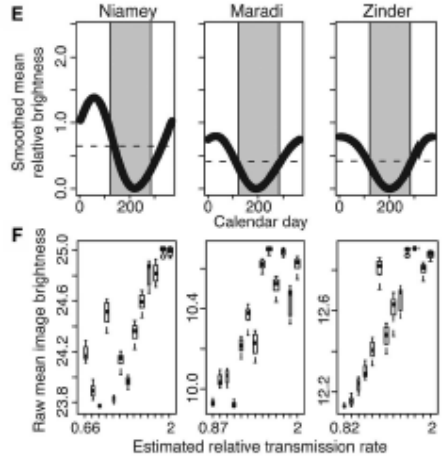
The dynamics of measles in sub-Saharan Africa

Matthew J. Ferrari[1], Rebecca F. Grais[2], Nita Bharti[3], Andrew J. K. Conlan[3], Ottar N. Bjørnstad[3,4], Lara J. Wolfson[5], Philippe J. Guerin[2], Ali Djibo[6] & Bryan T. Grenfell[3,4]

- Erratic epidemics
- Strong transmission seasonality might still help to predict the annual start of the outbreak
- regular, pulsed vaccine programmes may lead to more regular dynamics but are unlikely to eliminate major outbreaks until baseline vaccine levels reach high levels.

Science
AAAS

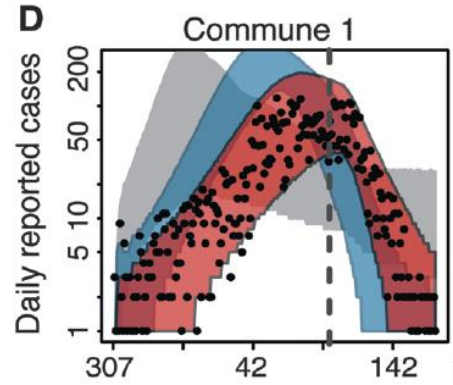
Explaining Seasonal Fluctuations of Measles in Niger Using Nighttime Lights Imagery
N. Bharti *et al.*
Science 334, 1424 (2011);
DOI: 10.1126/science.1210554



Reported measles cases

Science AAAS
Explaining Seasonal Fluctuations of Measles in Niger Using Nighttime Lights Imagery
N. Bharti *et al.*
Science 334, 1424 (2011);
DOI: 10.1126/science.1210554

- shading gives central 95% of predicted measles incidence from 25000 model simulations from
  - nighttime lights–informed model (red)
  - no migration model (blue)
  - constant migration model (gray).



- Dashed line indicates timing of outbreak response vaccination.

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→ **Conclusions**

Conclusions

- Seasonality can be a fundamental determinant of the dynamics of infectious diseases
  - Harmonic resonance and multi-year variability
  - Multiple, coexisting stable attractors, shift among them
  - Strength and shape of seasonality do matter
  - Seasonality might increase the peak/trough ratio and, under specific circumstances, foster stochastic fade out of the disease
- To exert the maximum effect, possibility of tuning up the timing of vaccination interventions so as to account for seasonal fluctuations
- Climate change might affect the dynamics of infectious diseases *also* through subtle but crucial changes in the strength and type of seasonality