SEIR models

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The SEIR model

The classic model for microparasite dynamics is the flow of hosts between **S**usceptible, **E**xposed (but not infectious) **I**nfectious and **R**ecovered compartments (Figure 1(a)). This leads to the following standard formulation of the $SEIR$ model

$$\frac{dS}{dt} = \mu(N[1-p] - S) - \frac{\beta IS}{N} \quad (1)$$

$$\frac{dE}{dt} = \frac{\beta IS}{N} - (\mu + \sigma)E \quad (2)$$

$$\frac{dI}{dt} = \sigma E - (\mu + \gamma)I \quad (3)$$

$$\frac{dR}{dt} = \gamma I - \mu R, \quad (4)$$

which makes a number of key biological assumptions:

- The basic $SEIR$ model represents infection dynamics in a total population of size N, with a natural 'background' death rate of all individuals balanced by a birth rate μN: from the sum of equations 2-4, $dN/dt = 0$ and $N = S + E + I + R$ is thus constant.
- The infection cause acute morbidity (not mortality); That is, relative to the lecture notes, we ignore disease induced mortality. This is reasonable for certain infections (like human measles) but not other examples (Dave will elaborate on Rabies tomorrow).
- Individuals are recruited directly into the susceptible class at birth.
- *Transmission* of infection from infectious to susceptible individuals is controlled by a bilinear contact term $\frac{\beta IS}{N}$. This is the simplest model for *mass action* transmission in a homogeneously-mixed host population. In particular, the scaling by population size (N) makes the reproduction ratio proportional to the local density of contacts and independent of population size.
- In the $SEIR$ model, Infected individuals move into the Exposed (not infectious) class after an average incubation period $1/\sigma$ and subsequently (if they escape natural mortality) through the infectious class after an average time $1/\gamma$. This deterministic approximation assumes an exponential distribution of incubation and infectious periods; though a tractable approximation for exploring overall dynamics, the observed duration of infection periods are of then much more nearly constant.
- The model assumes that recovered individuals are immune from infection (strictly to the ability to retransmit) for life;

In the absence of vaccination, the basic reproductive ratio, R_0, is $\frac{\sigma}{\sigma+\mu}\frac{\beta}{\gamma+\mu}$.

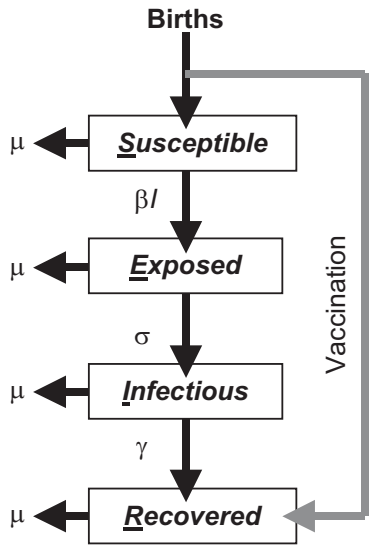


Figure 1: The SEIR flow diagram. Apart from vaccination, flows represent *per capita* flows from the donor compartment.

Numerical integration in R

We can use R to numerically integrate the SEIR model. We first define the grid of time step, parameters, and the starting conditions:

```
> times = seq(0, 10, by = 1/52)
> paras = c(mu = 1/75, N = 1, p = 0, beta = 1250, sigma = 365/7, gamma = 365/7)
> xstart = c(S = 0.06, E = 0, I = 0.001, R = 0)
```

and the function for the equation systems.

```
> seirmod = function(t, x, params) {
+     S = x[1]
+     E = x[2]
+     I = x[3]
+     R = x[4]
+     with(as.list(params), {
+         dS = mu * (N * (1 - p) - S) - beta * S * I/N
+         dE = beta * S * I/N - (mu + sigma) * E
+         dI = sigma * E - (mu + gamma) * I
+         dR = gamma * I - mu * R
+         res = c(dS, dE, dI, dR)
+         list(res)
+     })
+ }
```

To solve the ode's we need to use the odesolve library:

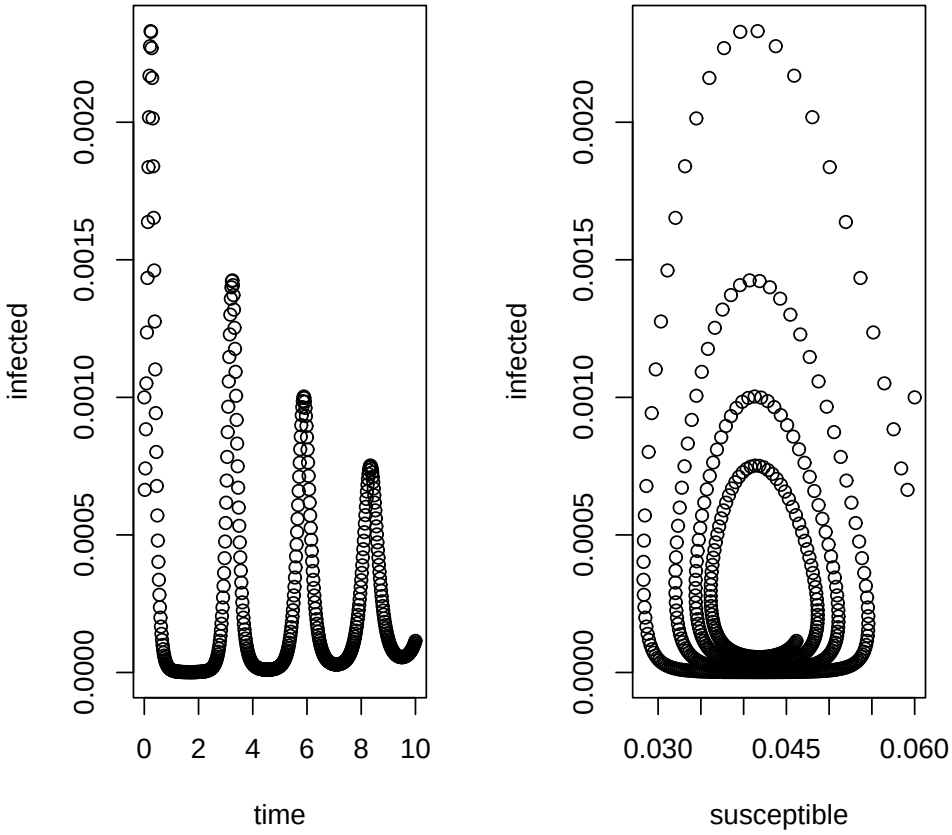
```
> library(odesolve)
```

Now integrate:

```
> out = as.data.frame(lsoda(xstart, times, seirmod, paras))
```

and plot as time series or as a phase space plot:

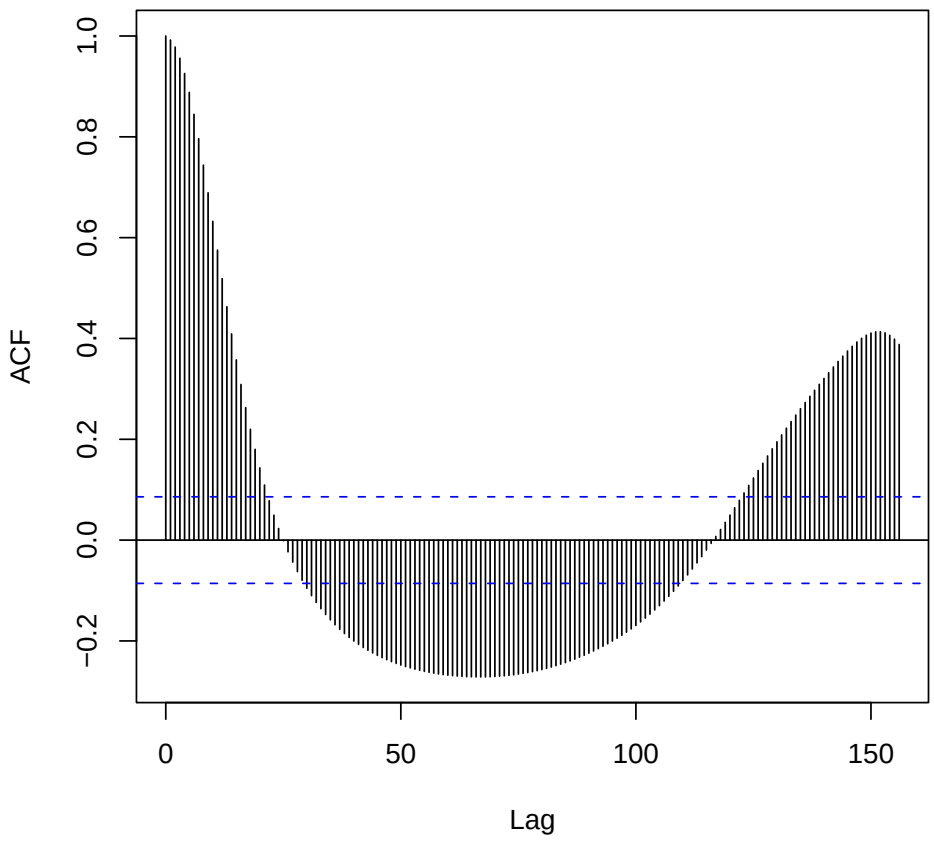
```
> par(mfrow = c(1, 2))
> plot(times, out$I, ylab = "infected", xlab = "time")
> plot(out$S, out$I, ylab = "infected", xlab = "susceptible")
```



Time series analysis

Spectral analysis and autocorrelation functions (ACF) are standard decriptive tools for time series analysis. ACF's calculates serial correlations at different time lags. For illustration, we can apply this to the (weekly) time series of prevalence that we generated above. In R we can do this for, say, lags up to 3 years (=156 weeks) by:

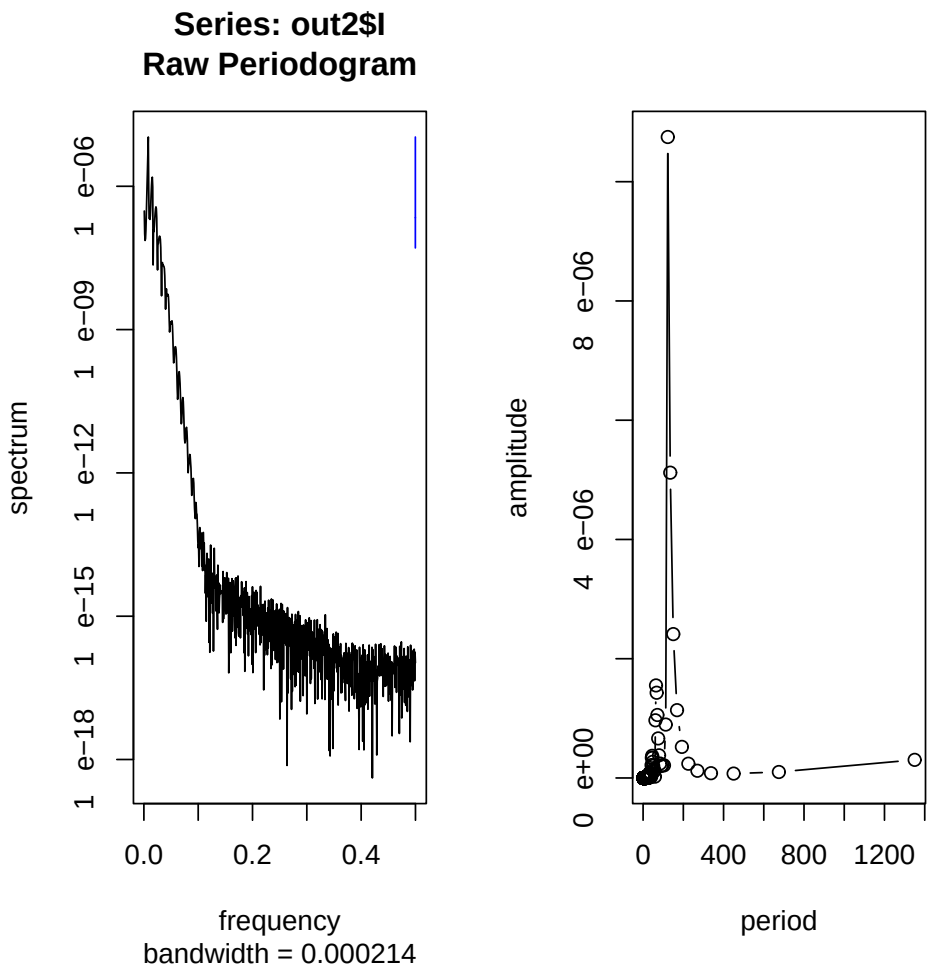
```
> par(mfrow = c(1, 1))
> acf(out$I, lag.max = 156)
```



The positive correlation at around 150 weeks gives an idea of a roughly 3 year periodicity in epidemic dynamics.

Periodograms (a type of spectral analysis) is a more direct way of estimating and testing for significant periodicity. The periodogram decomposes a time series into waves of different frequencies (frequency = 1/period). The importance of each frequency is measured by the spectral amplitude. We use the `spectrum`-function to calculate the periodogram for the epidemic series. Before we do this it is useful to generate a slightly longer simulation:

```
> times = seq(0, 25, by = 1/52)
> out2 = as.data.frame(lsoda(xstart, times, seirmod, paras))
> par(mfrow = c(1, 2))
> my.spec = spectrum(out2$I)
> plot(1/my.spec$freq, my.spec$spec, type = "b", xlab = "period", ylab = "amplitude")
```

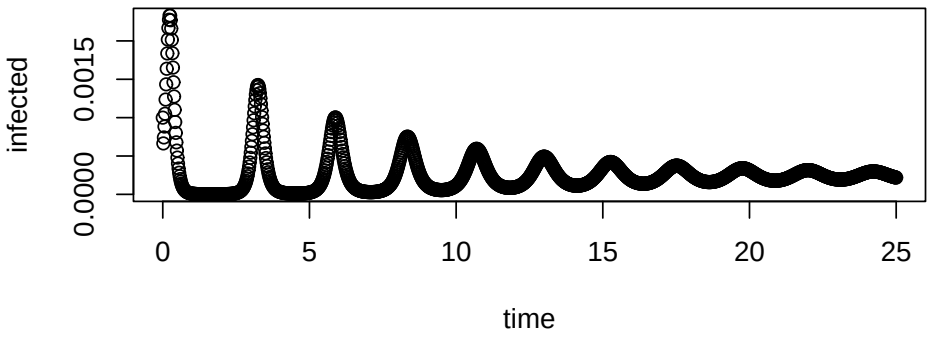


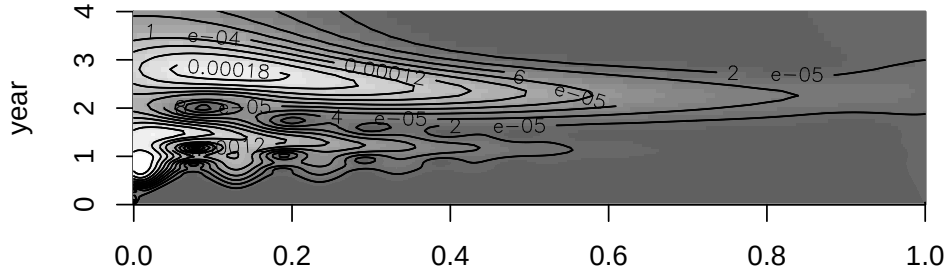
This analysis gives a clear illustration of the interepidemic period.

0.1 *special interest: wavelets

A recent extension of spectral analysis are the so-called Wavelet spectra that allows one to add a time axis to the periodogram (and therefore to allow for nonstationarities). In R wavelet spectra can be done using the `Rwave`-library:

```
> library(Rwave)
> par(mfrow = c(2, 1))
> plot(times, out2$I, xlab = "time", ylab = "infected")
> no = 8
> nv = 16
> j = 1:no
> k = (0:(nv - 1))/nv
> a = 2^apply(expand.grid(k, j), 1, sum)
> wfit = cwt(out2$I, no, nv, plot = F)
> tmp = Mod(wfit)
> image(tmp, col = gray((12:32)/32), y = a/52, ylim = c(0, 4), ylab = "year")
> contour(tmp, y = a/52, ylim = c(0, 4), zlim = c(mean(tmp), max(tmp)), add = TRUE)
```





We see that the interepidemic period is initially 3 years, but then decreases as the system converges on towards the stable endemic equilibrium.

1 Measles

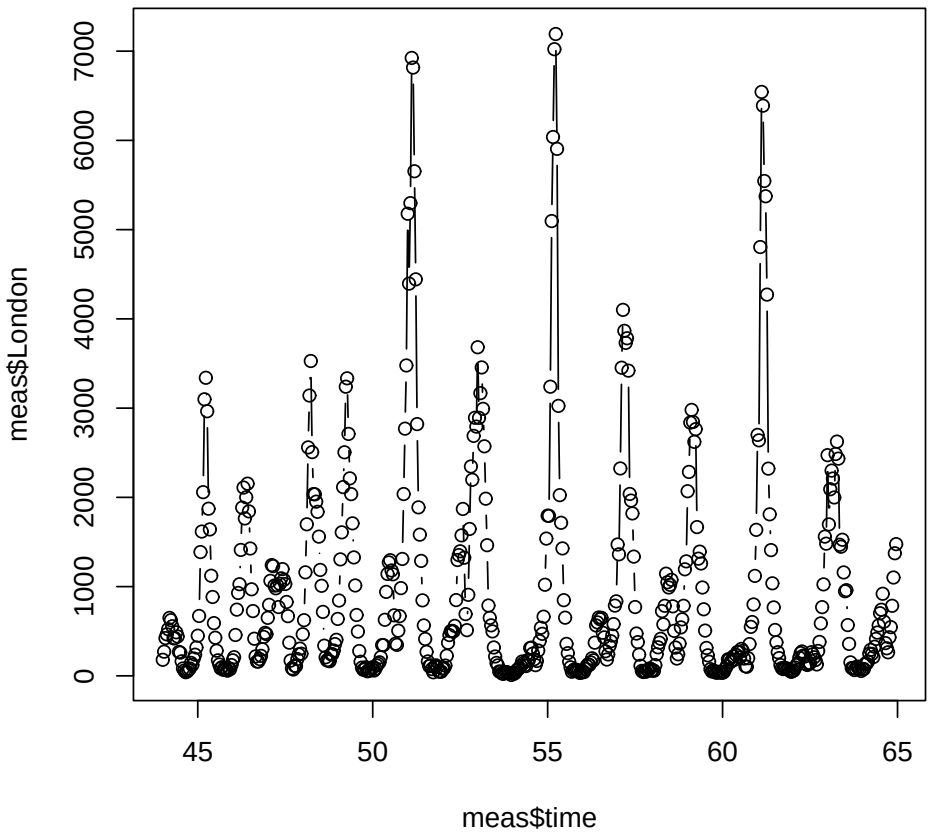
The biweekly incidence (number of cases for each two-week period) of measles has a long history in the study of infectious disease dynamics. The data set `meas.csv` contains the records from London between 1944 and 1966:

```
> meas = read.table("meas.csv", sep = ",", header = TRUE)
> names(meas)

[1] "year"   "week"   "time"   "London" "B"
```

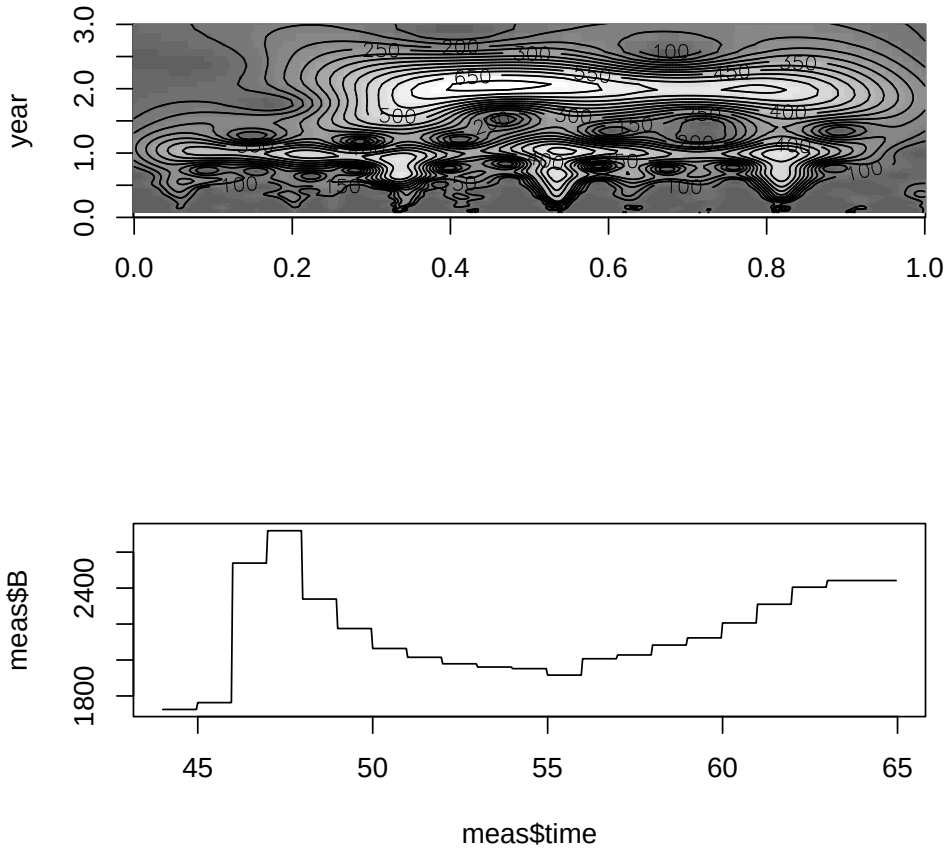
The incidence are accessed as `meas$London`. In addition, the data set contain columns reporting `meas$year`, `meas$month`, the two combined into `meas$time`, the incidence (`meas$London`), and biweekly number of births (`meas$B`).

```
> plot(meas$time, meas$London, type = "b")
```



We can use the time series methods to analyze the measles incidence data:

```
> no = 8
> nv = 16
> j = 1:no
> k = (0:(nv - 1))/nv
> a = 2^apply(expand.grid(k, j), 1, sum)
> wfit = cwt(meas$London, no, nv, plot = F)
> tmp = Mod(wfit)
> par(mfrow = c(2, 1))
> image(tmp, col = gray((12:32)/32), y = a/26, ylim = c(0, 3), ylab = "year")
> contour(tmp, y = a/26, ylim = c(0, 3), zlim = c(mean(tmp), max(tmp)), add = TRUE)
> plot(meas$time, meas$B, type = "l")
```



Historical measles incidence clearly exhibited a mixture of annual and biennial (two year) cycles; The two year cycles were more pronounced when birth rates were low. The early high birth rate years were associated with annual epidemics.