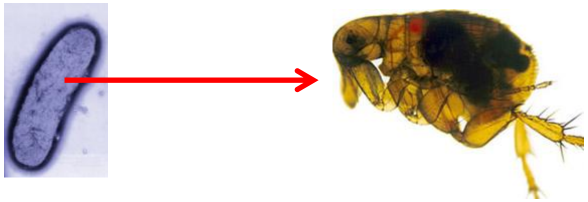
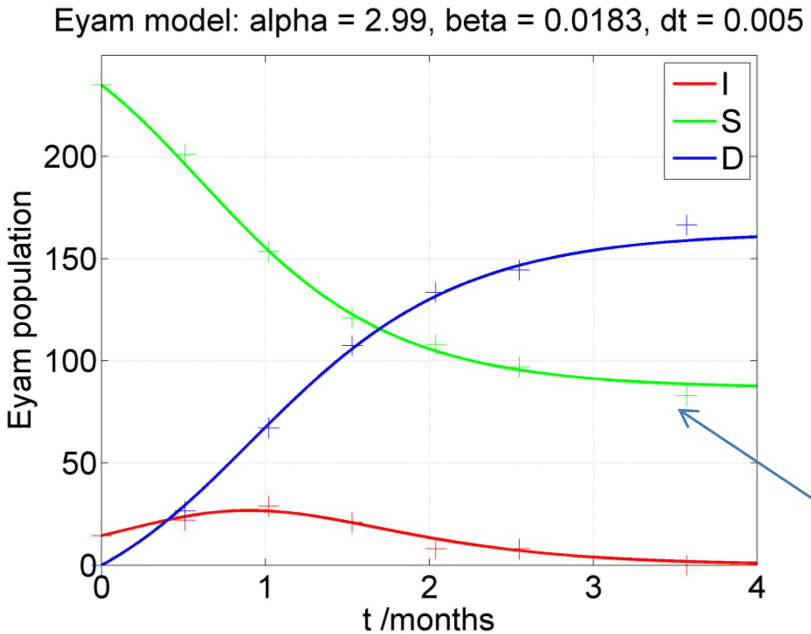
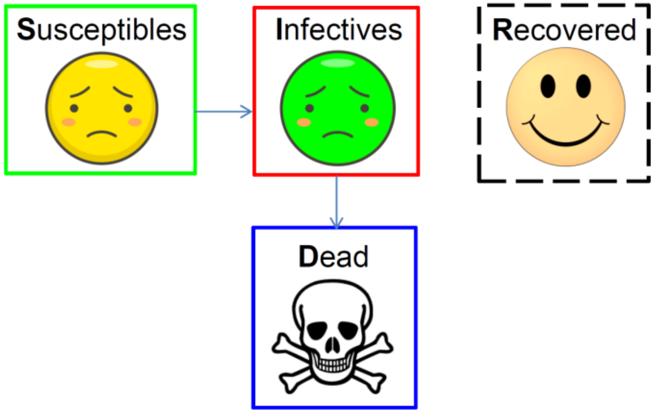
1665. A bale of damp cloth is delivered to the Derbyshire village of **Eyam**... George Viccars, the tailor's assistant, dries the cloth and releases fleas infected with *Yersinia Pestis* bacteria – **Plague**



Rector **William Mompesson** *quarantines* Eyam and records **Infected**, **Susceptible** and **Dead** populations *as time progresses*





Can we develop a mathematical model to predict I,S,D vs time? What does this tell us about *Epidemiology* in general?

e.g Flu, Ebola

Calculus methods, differential equations numerical methods, line of best fit, iteration, loops ...

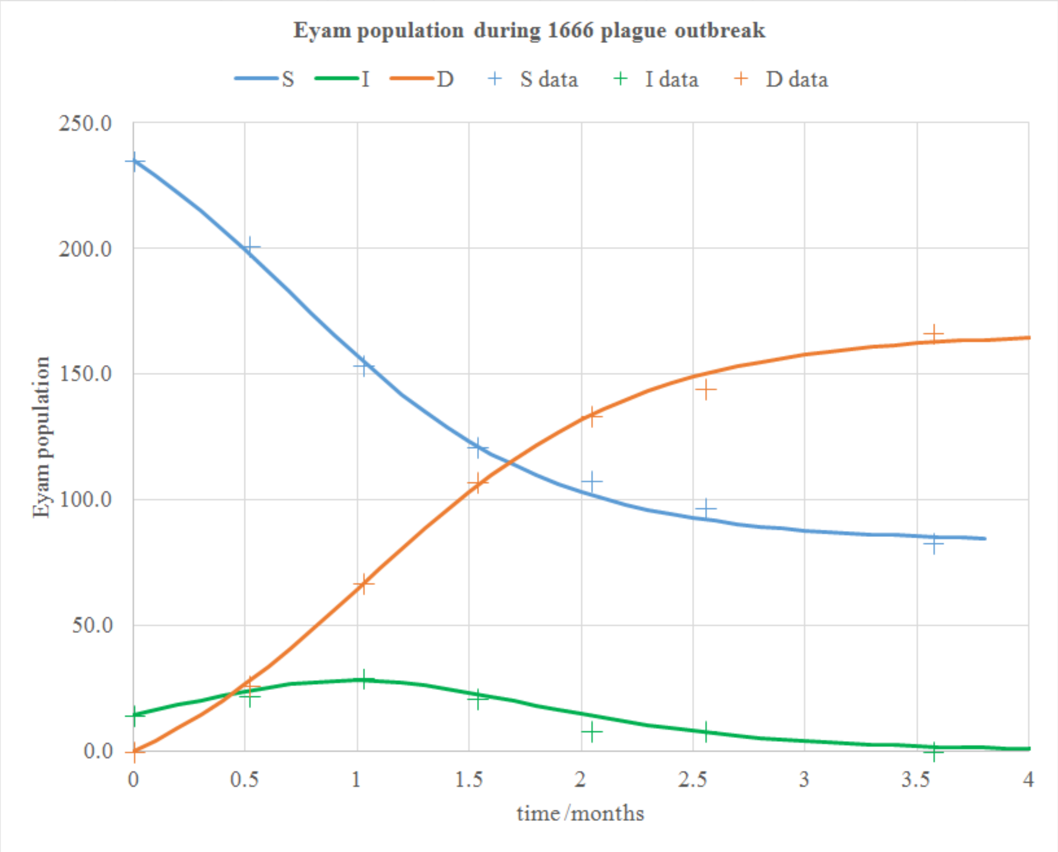
We performed the Eyam analysis in **Python**, then in **MATLAB**.
You can also construct an Euler model via a spreadsheet (**Excel**).

Black Death Epidemiological model using the Eyam data

Andy French & John Cullerne. 24th February 2018.

Initial population N0	249.5
Initial number of succeptables S0	**235**
Initial number of infectives I0	**14.5**
Transmission rate constant beta	0.017759
Death rate constant alpha	**2.9**
timestep dt /months	**0.1**

t /months	S	I	D	N	N+D = N0
0	235.0	14.5	0.0	249.5	249.5
0.1	228.9	16.3	4.2	245.3	249.5
0.2	222.3	18.3	8.9	240.6	249.5
0.3	215.1	20.2	14.2	235.3	249.5
0.4	207.4	22.0	20.1	229.4	249.5
0.5	199.3	23.7	26.5	223.0	249.5
0.6	190.9	25.3	33.4	216.1	249.5
0.7	182.3	26.5	40.7	208.8	249.5
0.8	173.7	27.4	48.4	201.1	249.5
0.9	165.3	27.9	56.3	193.2	249.5
1	157.1	28.0	64.4	185.1	249.5
1.1	149.3	27.7	72.5	177.0	249.5
1.2	141.9	27.0	80.6	168.9	249.5
1.3	135.1	26.0	88.4	161.1	249.5
1.4	128.9	24.7	95.9	153.6	249.5
1.5	123.3	23.2	103.1	146.4	249.5
1.6	118.2	21.5	109.8	139.7	249.5



$$\frac{dS}{dt} = -\beta SI \qquad \frac{dI}{dt} = \beta SI - \alpha I \qquad \frac{dD}{dt} = \alpha I$$

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dI}{dt} = \beta SI - \alpha I$$

$$\frac{dD}{dt} = \alpha I$$

Leonhard Euler
1707-1783

Euler numerical *iterative* solution scheme

$$\alpha = 2.894, \quad \beta = \frac{\alpha}{163.3}$$

$$t_0 = 0, \;\; S_0 = 235, \;\; I_0 = 14.5, \;\; D_0 = 0$$

$$t_{n+1} = t_n + \Delta t$$

$$S_{n+1} = S_n - \beta S_n I_n \Delta t$$

$$I_{n+1} = I_n + \left(\beta S_n I_n - \alpha I_n\right)\Delta t$$

$$D_{n+1} = D_n + \alpha I_n \Delta t$$

i.e. fix a time interval and work out what happens after each time step.

```matlab
%Euler method solver for differential equations which
%describe model of Eyam epidemic.
function [t,I,S,D] = eyam_model( dt, I0, S0, alpha, beta, tmax )

%Initialize output vectors for t,I,S,D
t = 0 : dt : tmax;
N = length(t);
S = S0*ones(1,N);
I = I0*ones(1,N);
D = zeros(1,N);

%Loop through vectors to compute t, I, S, D.
%using the Euler first order differential equation method
for n=2:N
    t(n) = t(n-1) + dt;
    I(n) = I(n-1) + dt*( beta*S(n-1)*I(n-1) - alpha*I(n-1) );
    S(n) = S(n-1) - dt*beta*S(n-1)*I(n-1);
    D(n) = D(n-1) + dt*alpha*I(n-1);
end
```

$$\alpha = 2.894, \quad \beta = \frac{\alpha}{163.3}$$

$$t_0 = 0, \; S_0 = 235, \; I_0 = 14.5, \; D_0 = 0$$

$$t_{n+1} = t_n + \Delta t$$

$$S_{n+1} = S_n - \beta S_n I_n \Delta t$$

$$I_{n+1} = I_n + \left(\beta S_n I_n - \alpha I_n\right)\Delta t$$

$$D_{n+1} = D_n + \alpha I_n \Delta t$$

MATLAB code for Euler Eyam model

$$\frac{dS}{dt} = -\beta SI, \quad \frac{dI}{dt} = \beta SI - \alpha I$$

$$\therefore \frac{dI}{dS} = -\frac{\beta SI - \alpha I}{\beta SI} = \tfrac{\alpha}{\beta}\frac{1}{S} - 1$$

$$\therefore I - I_0 = \int_{S_0}^{S}\left(\tfrac{\alpha}{\beta}\frac{1}{S} - 1\right)dS = \left[\tfrac{\alpha}{\beta}\ln S - S\right]_{S_0}^{S}$$

$$I = I_0 + \tfrac{\alpha}{\beta}\ln\frac{S}{S_0} - S + S_0$$

$$\tfrac{\alpha}{\beta}\underset{x}{\ln\frac{S_0}{S}} = \underbrace{I_0 + S_0 - I - S}_{y}$$

$$\therefore y = \tfrac{\alpha}{\beta}x$$

Eyam Equations

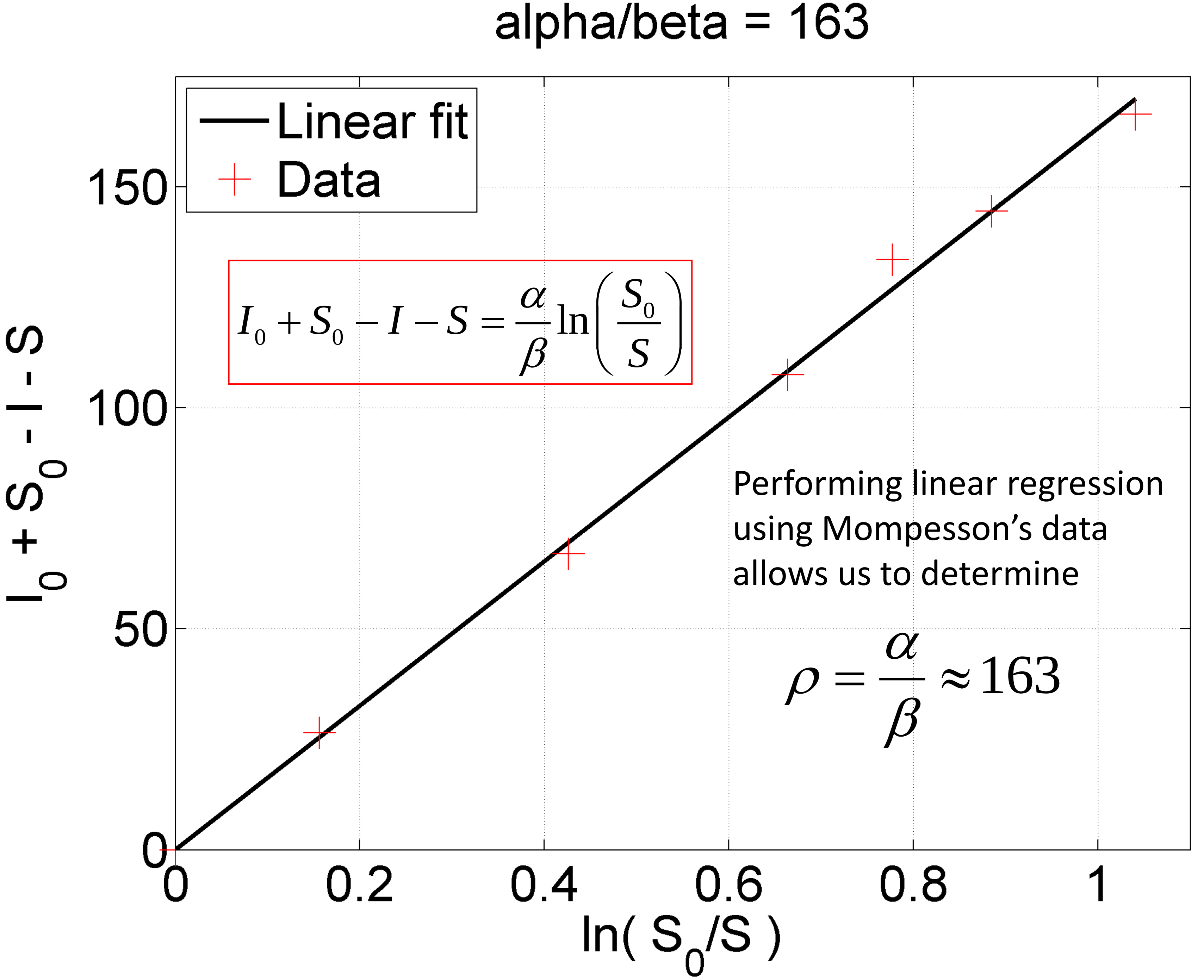
$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dD}{dt} = \alpha I$$

$$\frac{dI}{dt} = \beta SI - \alpha I$$

Note we can integrate to find *I(S)* analytically

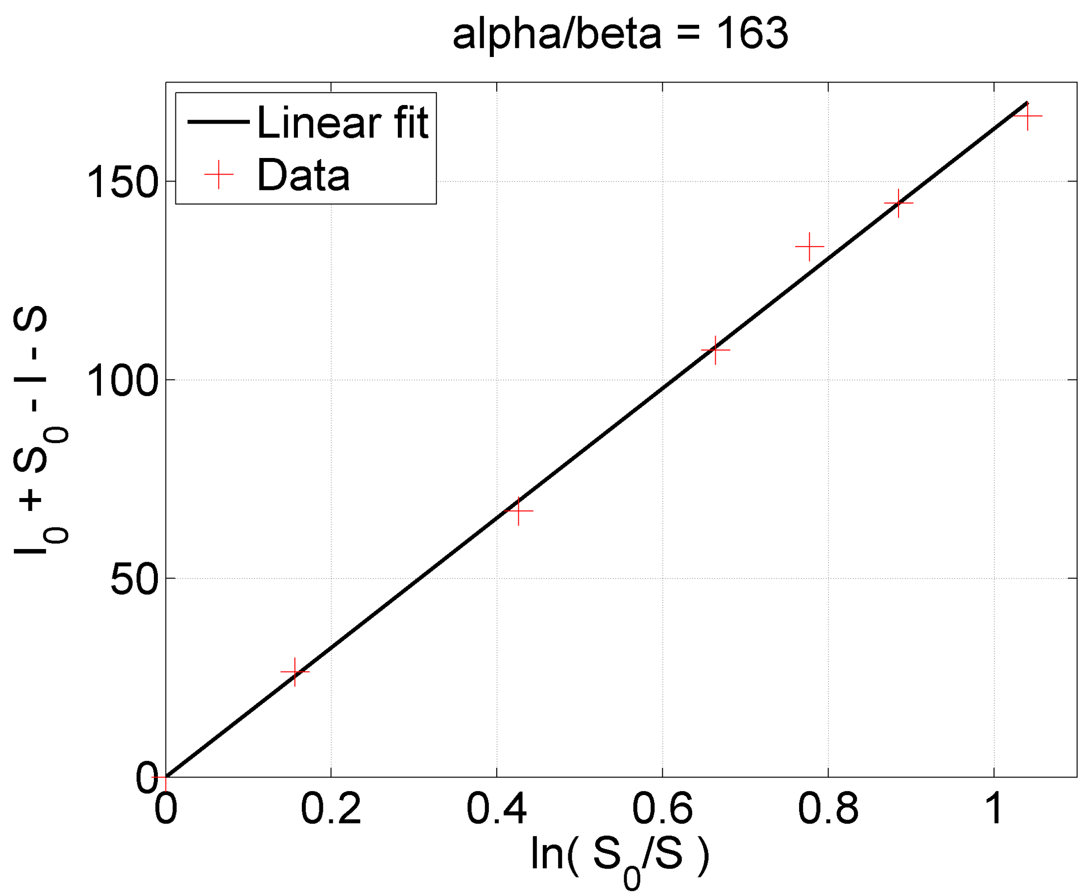
.... But not *I(t)*, *S(t)*, *D(t)*

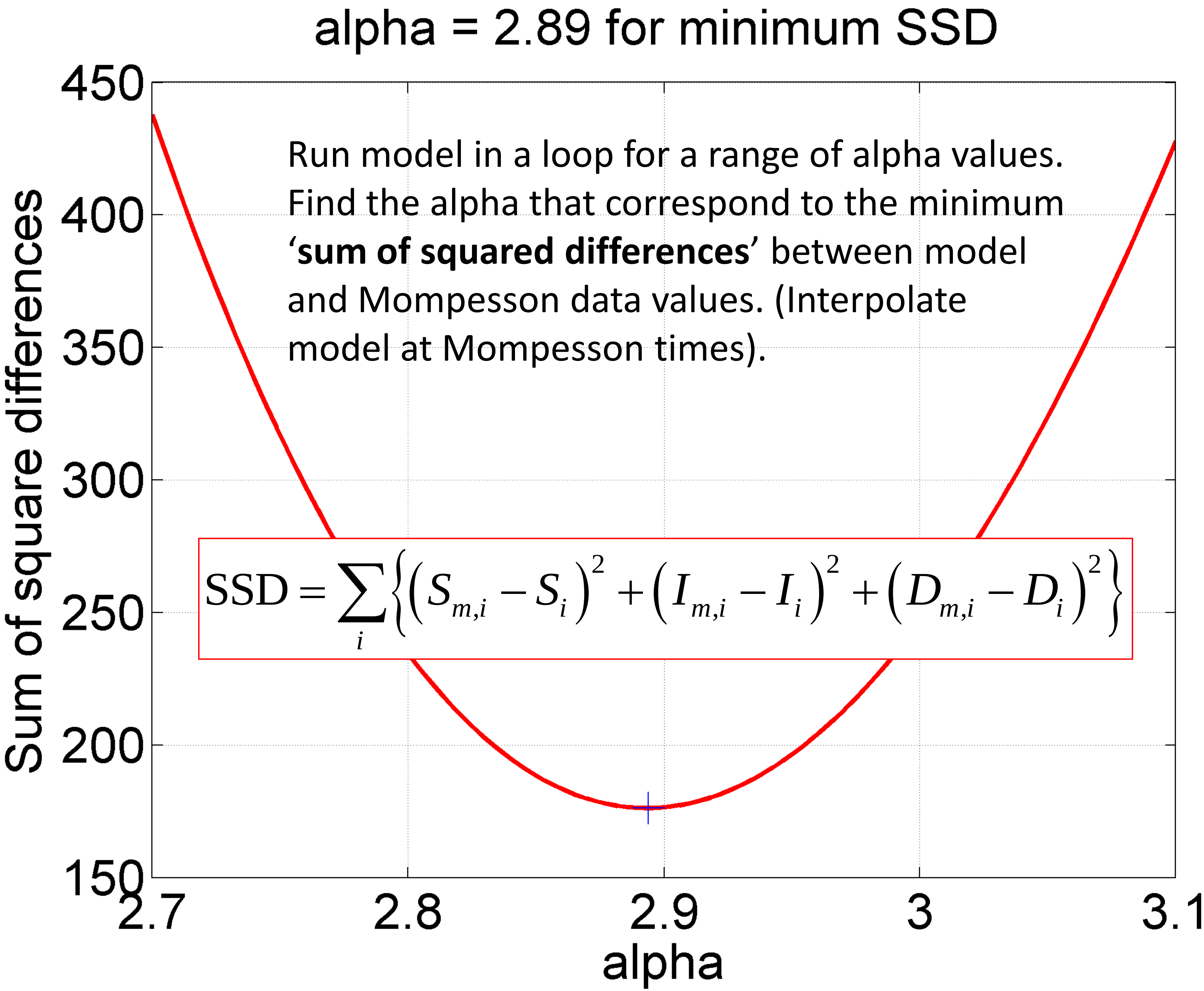

alpha/beta = 163
Linear fit
Data
$$I_0 + S_0 - I - S = \frac{\alpha}{\beta}\ln\left(\frac{S_0}{S}\right)$$
Performing linear regression using Mompesson's data allows us to determine
$$\rho = \frac{\alpha}{\beta} \approx 163$$
$I_0 + S_0 - I - S$
$\ln(S_0/S)$
0
50
100
150
0
0.2
0.4
0.6
0.8
1

```
%Line of best fit function yfit = m*x, with product moment correlation
%coefficient r
function [yfit,xfit,r,m] = bestfit(x,y)

%Find any x or y values that are NaN or Inf
ignore = isnan(abs(x)) | isnan(abs(y)) | isinf(abs(x)) | isinf(abs(y));
x(ignore) = [];
y(ignore) = [];

%Compute line of best fit
xybar = mean(x.*y);
xxbar = mean(x.^2 );
yybar = mean(y.^2 );
m = xybar/xxbar;
r = xybar/( xxbar*yybar );
yfit = m*x;
xfit = x;
```

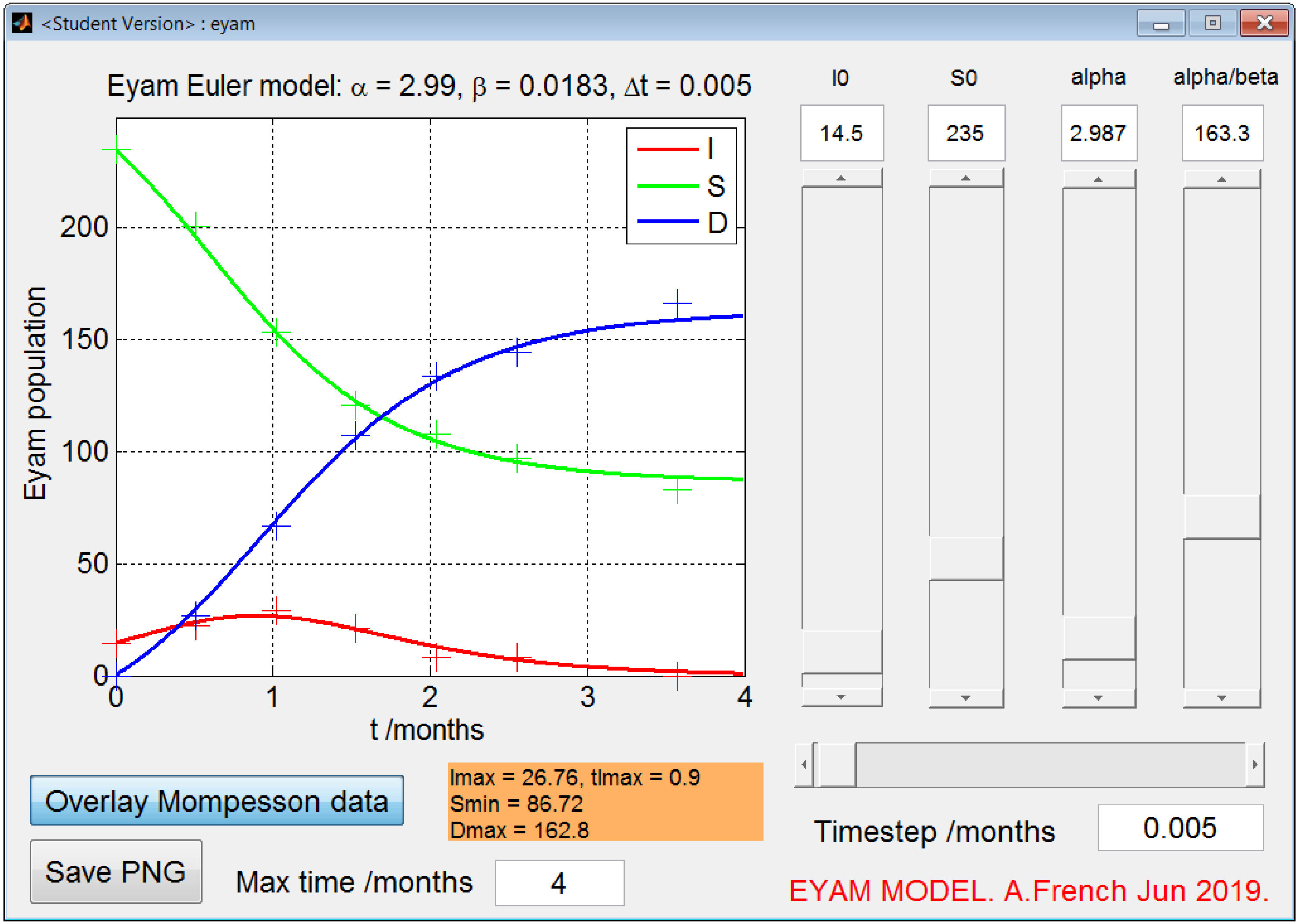


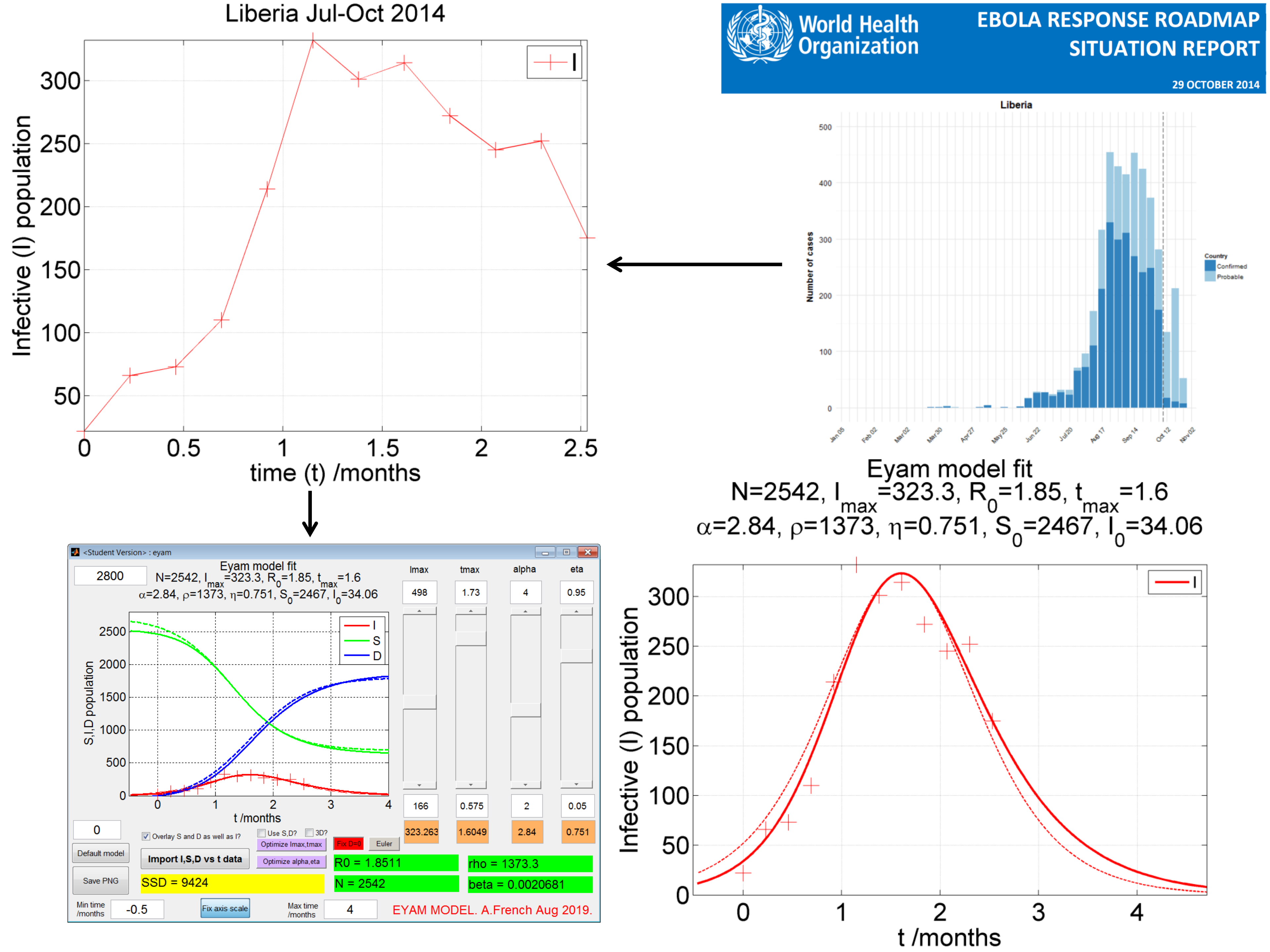


Run model in a loop for a range of alpha values. Find the alpha that correspond to the minimum '**sum of squared differences**' between model and Mompesson data values. (Interpolate model at Mompesson times).

$$\mathrm{SSD} = \sum_i \left\{ \left(S_{m,i} - S_i\right)^2 + \left(I_{m,i} - I_i\right)^2 + \left(D_{m,i} - D_i\right)^2 \right\}$$

Euler Eyam solver implemented in MATLAB with a **Graphical User Interface** (GUI). Change the inputs via the sliders or edit boxes, and the curves are computed automatically.





Liberia Jul-Oct 2014
Infective (I) population
time (t) /months
I
World Health Organization
EBOLA RESPONSE ROADMAP
SITUATION REPORT
29 OCTOBER 2014
Liberia
Number of cases
Country
Confirmed
Probable
Eyam model fit
N=2542, I_max=323.3, R_0=1.85, t_max=1.6
α=2.84, ρ=1373, η=0.751, S_0=2467, I_0=34.06
Infective (I) population
t /months
<Student Version> : eyam
2800
Imax
tmax
alpha
eta
498
1.73
4
0.95
S,I,D population
t /months
I
S
D
166
0.575
2
0.05
323.263
1.6049
2.84
0.751
0
Overlay S and D as well as I?
Use S,D?
3D?
Optimize Imax,tmax
Fix D=0
Euler
Default model
Import I,S,D vs t data
Optimize alpha,eta
R0 = 1.8511
rho = 1373.3
Save PNG
SSD = 9424
N = 2542
beta = 0.0020681
Min time /months
-0.5
Fix axis scale
Max time /months
4
EYAM MODEL. A.French Aug 2019.

$$z_{+} = -\ln(1-\eta) - \ln\left(-\frac{\ln(1-\eta)}{\eta}\right)$$

$$z_{-} = -\ln\left(-\frac{\ln(1-\eta)}{\eta}\right)$$

$$x_{\max} = -\frac{\ln(1-\eta)}{\eta} - 1 - \ln\left(-\frac{\ln(1-\eta)}{\eta}\right)$$

$$\rho = \frac{I_{\max}}{x_{\max}}$$

$$\tau(z) = \int_0^z \frac{dz'}{x_{\max} + 1 - e^{-z'} - z'}$$

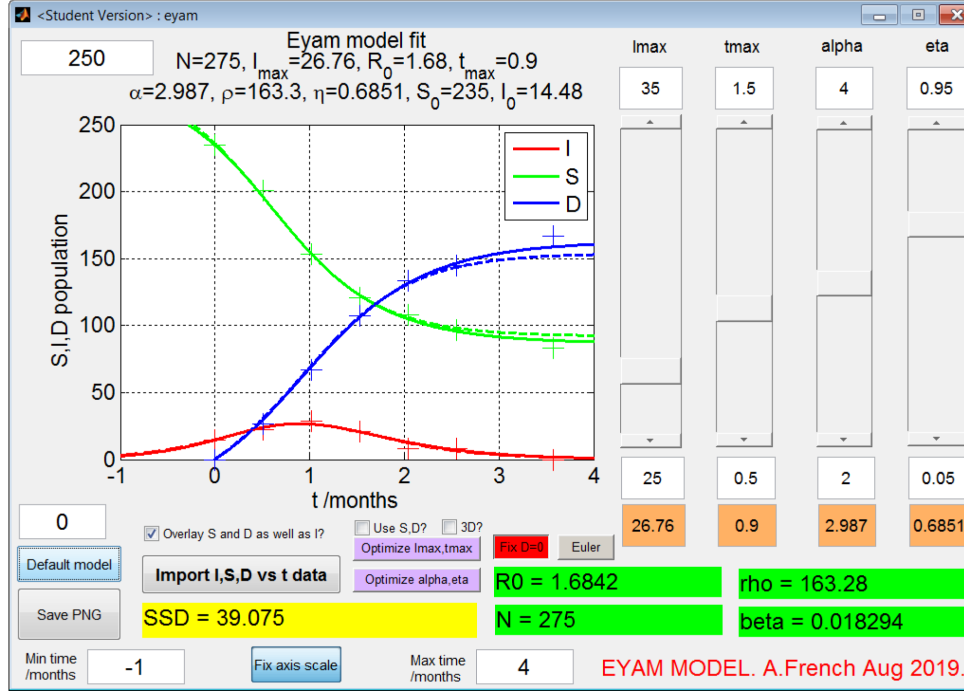
$$x = x_{\max} + 1 - e^{-z} - z$$

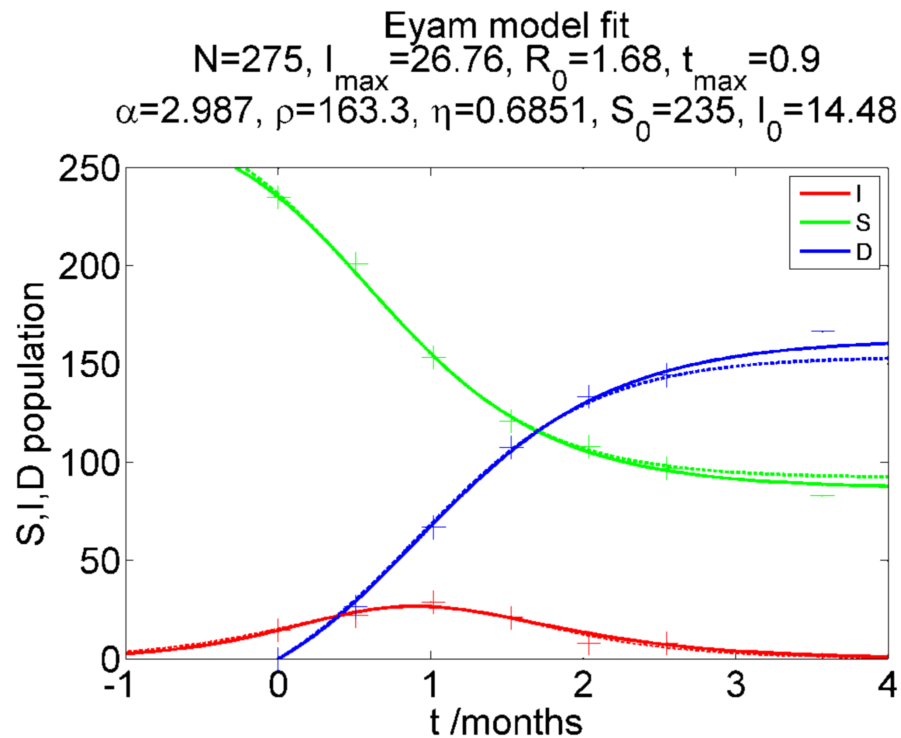
$$y = e^{-z}$$

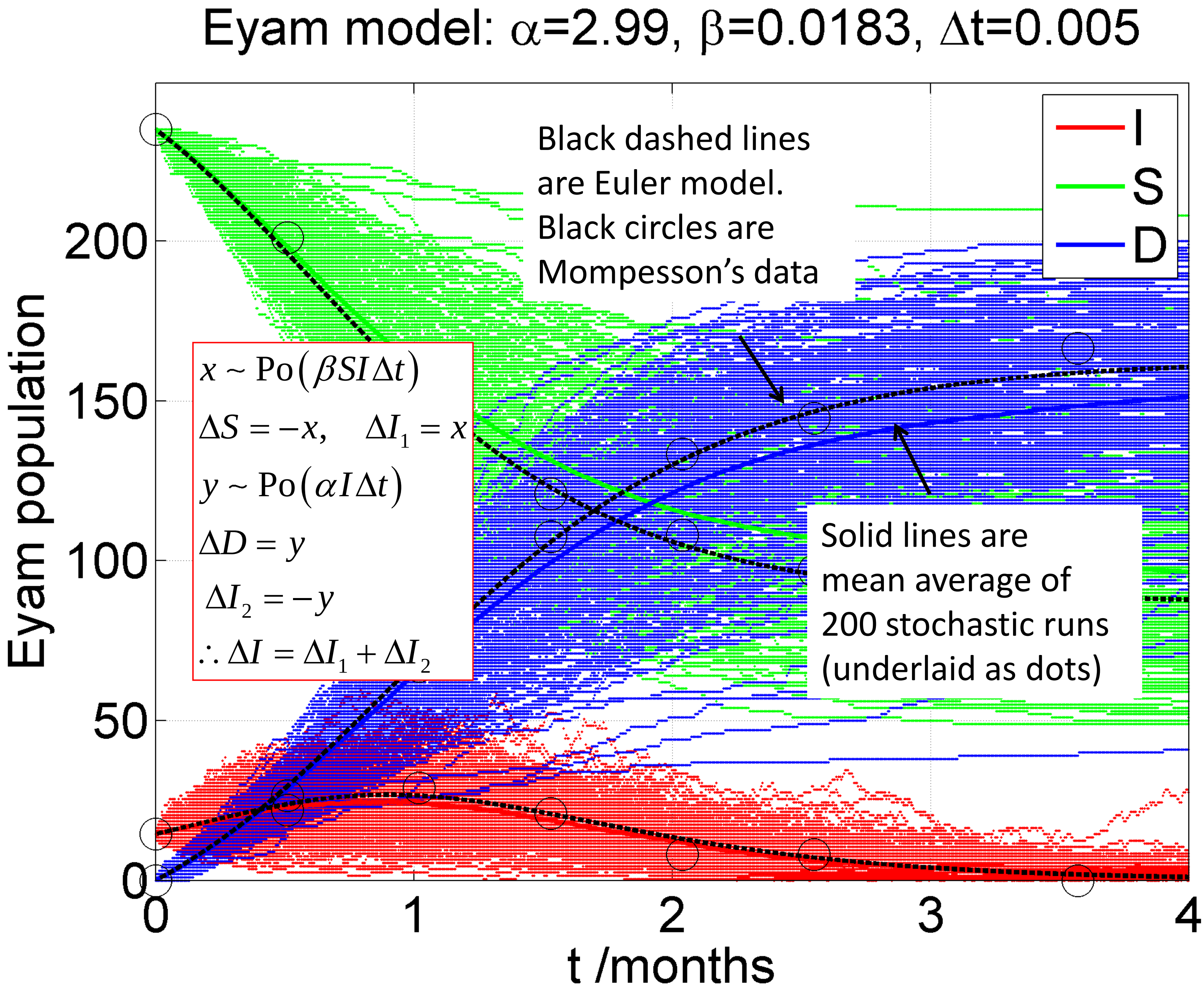
$$t = \frac{\tau}{\alpha} + t_{\max}, \quad I = \rho x \quad S = \rho y, \quad D = \rho(z - z_{-})$$

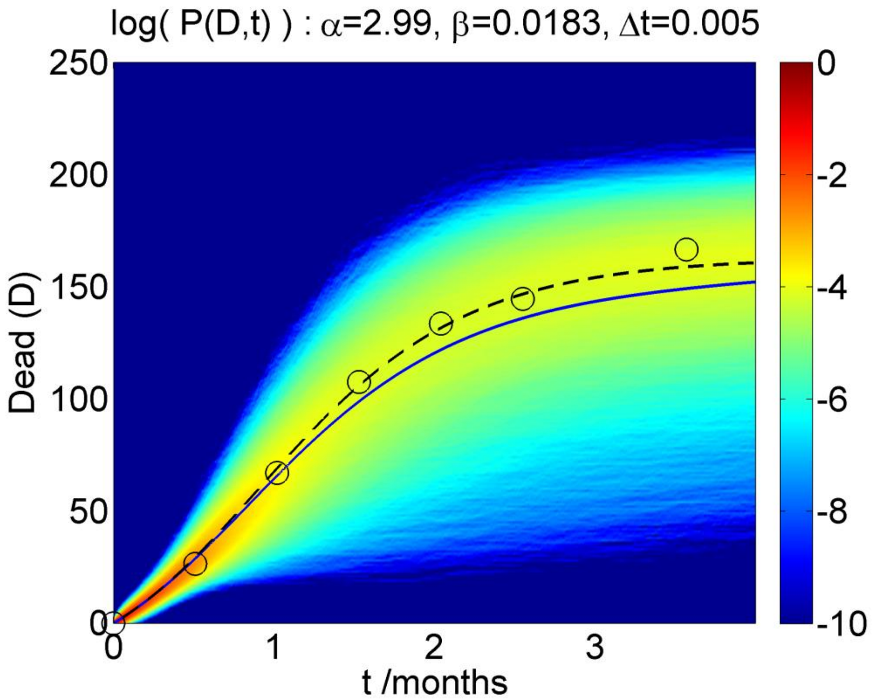
$$N = I_{\max} + \rho - \rho z_{-}$$

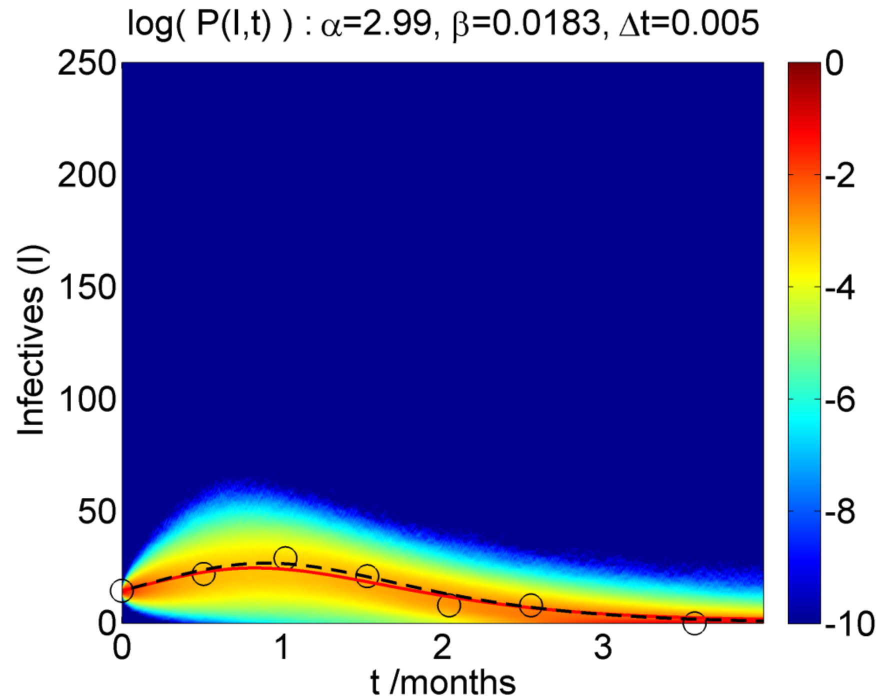
$$R_0 = \frac{N}{\rho}$$

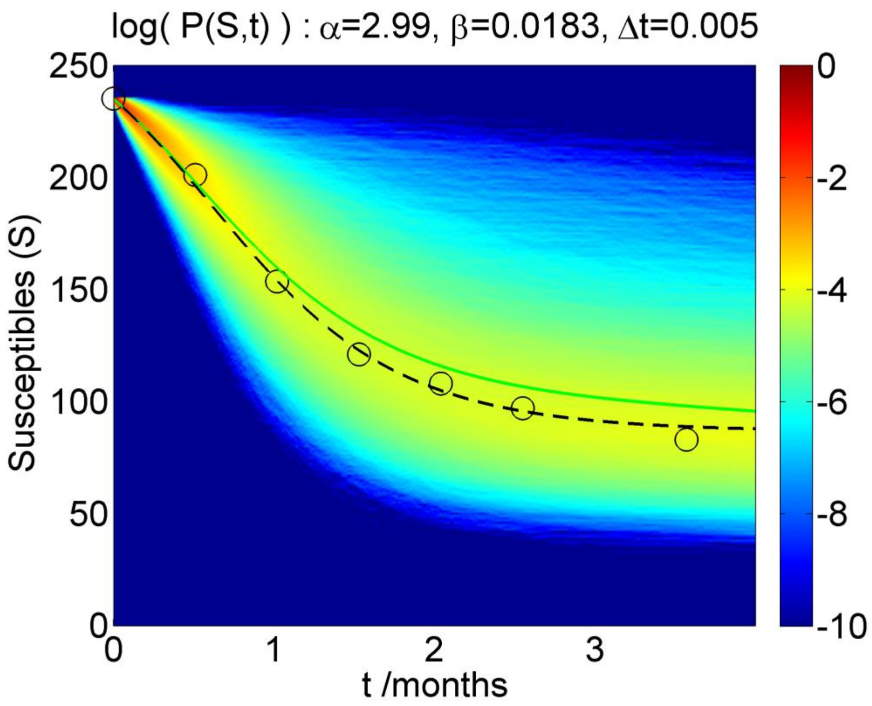




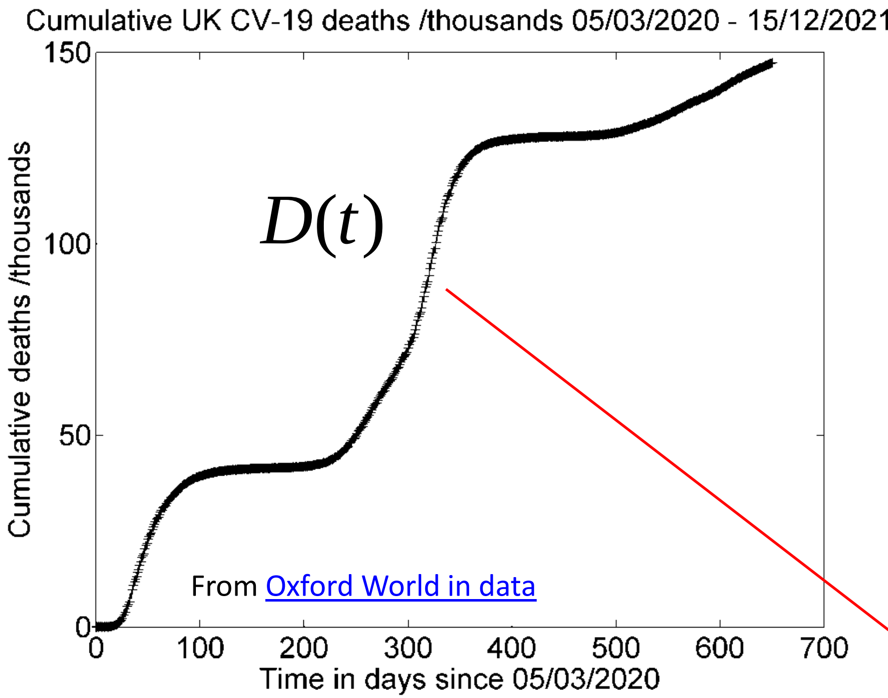

Eyam model: α=2.99, β=0.0183, Δt=0.005
Eyam population
t /months
0
50
100
150
200
0
1
2
3
4
I
S
D
Black dashed lines are Euler model. Black circles are Mompesson's data
Solid lines are mean average of 200 stochastic runs (underlaid as dots)
$x \sim \text{Po}(\beta S I \Delta t)$
$\Delta S = -x, \quad \Delta I_1 = x$
$y \sim \text{Po}(\alpha I \Delta t)$
$\Delta D = y$
$\Delta I_2 = -y$
$\therefore \Delta I = \Delta I_1 + \Delta I_2$



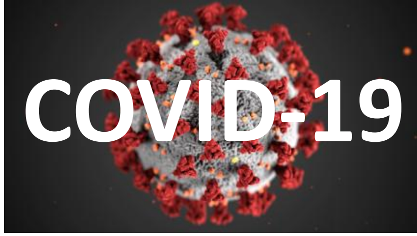




Probability map computed from 50,000 iterations. Black circles are from the Mompesson Plague data set and black dashed lines correspond to the Euler model.



One can *estimate* the number of CV-19 **infectives** from the cumulative deaths:

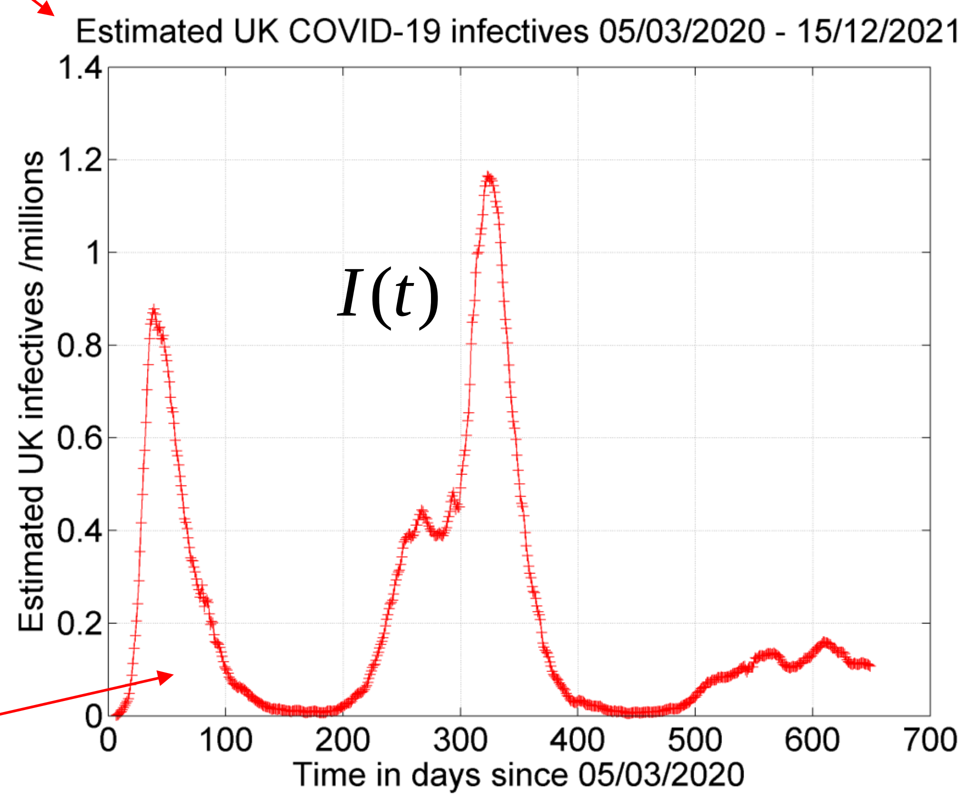


$$I_n = \frac{1}{k\alpha}\frac{dD}{dt} \approx \frac{1}{k\alpha}\frac{D_{n+1} - D_{n-1}}{t_{n+1} - t_{n-1}}$$

Find the gradient and scale by:

$$k\alpha = 0.01 \times \frac{1}{9.32} \text{ days}^{-1}$$

Note *mortality fraction k* and *disease time constant α* may vary considerably within a population and indeed post-vaccination – so treat with caution!



Note: as per the 'daily death rate' graphs in *World in Data*, we also apply a **seven-day moving average** to smooth the numerical derivative.