A stochastic model for the transmission of 2019-nCov in Wuhan

John M. Drake

1/25/2020

Introduction

The epidemiology of the 2019-nCov in China is poorly understood. Here we seek to develop a model for the transmission of 2019-nCov during the early stages of transmission in Wuhan. This model may be useful for inference, forecasting or scenario analysis.

Strategy

1. Develop a generative model based on clinical reports and outbreak investigations reported in the media and scientific literature.
2. Estimate unknown parameters by fitting to data.
3. Application of model to specific problems such as characterizing key unknown quantities (e.g. reporting rate) and forecasting.

Model construction

Up to approximately January 25 the outbreak has remained small (hundreds of cases). Therefore, we adopt a stochastic modeling approach that reflects intrinsic noise. The model will be constructed for simulation via Gillespie's direct method. Additionally, we assume that the primary model compartments are Susceptible, Infected, and Recovered individuals. Given that the epidemic is an acute infection with dynamics that occur on time scales much faster than the demography of the population, we assume a *closed* population. Additional, we recognize that the waiting time distributions are not exponential and therefore use the Linear Chain Trick (LCT) to represent realistic wait times in each compartment (Cite: https://link.springer.com/article/10.1007/s00285-019-01412-w) From (https://github.com/jabacker/nCoV-2019/blob/master/Incubationperiod_2019nCoV.pdf), the incubation period is gamma distributed with a mean of 5.6 days and shape parameter 6.2. For simplicity, we assume an Erlang distribution with integer shape parameter of 6. Thus, we require six exposed classes.

We do not yet have a model for the time in the infectious class. Indeed, we will seek to let this rate be a function of time itself to recognize the effect of case identification and isolation, social distancing, etc. For now, we will again assume an Erland distribution with integer shape parameter of 6.

The basic function simulates one event in the transmission process.

For now, the model assumes a frequency-dependent force of infection of $\lambda = \beta \times Y/N$. This is reasonable for a respiratory infection that requires relatively close contact for infection to occur (compare: https://science.sciencemag.org/content/362/6410/75) **Ultimately, we hope to transfer estimates among different locations, therefore a force of infection that is intermediate between density-dependent and frequency-dependent transmission should be considered a high priority for further development.**

```
onestep <- function (x, params) {  #function to calculate one step of stochastic SIR
  S <- x[2]                        #local variable for susceptibles

  E1 <- x[3]                       #exposed classes
```

```
  E2 <- x[4]
  E3 <- x[5]
  E4 <- x[6]
  E5 <- x[7]
  E6 <- x[8]

  I1 <- x[9]                          #infectious classes
  I2 <- x[10]
  I3 <- x[11]
  I4 <- x[12]
  I5 <- x[13]
  I6 <- x[14]

  I <- I1+I2+I3+I4+I5+I6

  R <- x[15]                         #local variable for recovereds
  N <- S+E1+E2+E3+E4+E5+E6+I1+I2+I3+I4+I5+I6+R                          #total population size (subjec
  with(                               #use with as in deterministic model to simplify code
       as.list(params),
       {
         rates <- c(beta*S*I/N,
                    sigma*E1, sigma*E2, sigma*E3, sigma*E4, sigma*E5, sigma*E6,
                    gamma*I1, gamma*I2, gamma*I3, gamma*I4, gamma*I5, gamma*I6)
         changes <- matrix(c(-1, 1, 0, 0, 0, 0, 0 ,0, 0, 0, 0, 0, 0, 0,   #transition into E
                             0, -1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
                             0, 0, -1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
                             0, 0, 0, -1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0,
                             0, 0, 0, 0, -1, 1, 0, 0, 0, 0, 0, 0, 0, 0,
                             0, 0, 0, 0, 0, -1, 1, 0, 0, 0, 0, 0, 0, 0,

                             0, 0, 0, 0, 0, 0, -1, 1, 0, 0, 0, 0, 0, 0,   #transition into I
                             0, 0, 0, 0, 0, 0, 0, -1, 1, 0, 0, 0, 0, 0,
                             0, 0, 0, 0, 0, 0, 0, 0, -1, 1, 0, 0, 0, 0,
                             0, 0, 0, 0, 0, 0, 0, 0, 0, -1, 1, 0, 0, 0,
                             0, 0, 0, 0, 0, 0, 0, 0, 0, 0, -1, 1, 0, 0,
                             0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, -1, 1, 0,

                             0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, -1, 1),  #transitions into R
                           ncol=length(x)-1, byrow=TRUE)
         tau <- -log(runif(1)) / sum(rates)   # exponential waiting time
         U <- runif(1)       #uniform random deviate
         m <- min(which(cumsum(rates)>=U*sum(rates)))
         x <- x[2:length(x)] + changes[m,]
         return(out <- c(tau, x))
       }
       )
}
```

A second function iteratively applies `onestep` to evaluate a solution of the model.

```
model <- function (x, params, nstep) {  #function to simulate stochastic SIR
  output <- array(dim=c(nstep+1,length(x)))         #set up array to store results
  colnames(output) <- c("time","S",
                        "E1", "E2", "E3", "E4", "E5", "E6",
```

```
                        "I1", "I2", "I3", "I4", "I5", "I6",
                        "R") #name variables
  output[1,] <- x                          #first record of output is initial condition
  for (k in 1:nstep) {                     #iterate for nstep steps
    output[k+1,] <- x <- onestep(x,params)
  }
  output                                   #return output
}
```

A third function simulates an arbitrary number of realizations, stores and plots the result.

All units are expressed in terms of days. Note that the mean of a gamma distributed random variable (incubation period, infectious period) is given by $\mu = k/r$ where k is the shape parameter and r is the rate. Thus, since we have assumed $k = 6$ for both the incubation period and infectious period, these are considered in the parameterization below.

Parameters are as follows:

Population size of Wuhan: $N \approx 11081000$ (Wikipedia)

We assume $R_0 = 2.6$ as a notional value (Imperial College estimate)

Recovery rate (assuming seven day infectious period): $\gamma = 6/7$

Transmissibility: $\beta = R_0 \times \gamma \approx 3.7$ **Note: A better estimate of β might be obtained by measuring the takeoff rate and calculating according to Wearing & Rohani (https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0020174#pmed-0020174-e004)**

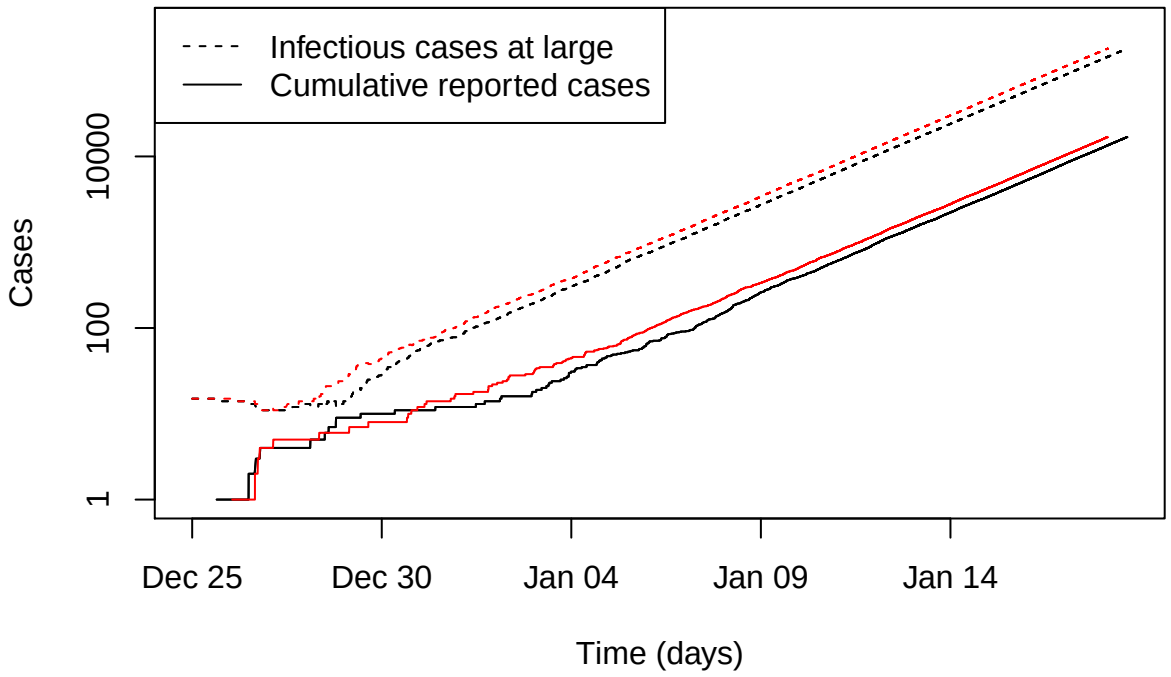
Transition through incubation period (Becker): $\sigma = 6/5.6$

Simulations

Here we evaluate the model. Note that this model assumes that all infectious cases are eventually reported. The difference between infectious cases in the community and reported cases simply reflect the lag between infection and isolation. For this simulation it is assumed that the initial number of infectious cases is 15 (the reported size of the initial cluster) distributed over the first three infectious pseudo-classes. The model is presumed to start on December 25.

```
start <- as.Date('12/25/2019',format='%m/%d/%Y')

set.seed(1252019)                #set seed

evaluate.model <- function(params=list(beta=3.7, gamma=6/7, sigma=6/5.6), nsims=2, pop.size=11081000, ns

  E10 <- 0
  E20 <- 0
  E30 <- 0
  E40 <- 0
  E50 <- 0
  E60 <- 0

  E0 <- E10+E20+E30+E40+E50+E60

  I10 <- 3
  I20 <- 3
  I30 <- 3
  I40 <- 3
```

```
  I50 <- 3
  I60 <- 0

  I0 <- I10+I20+I30+I40+I50+I60

  S0 <- round(pop.size-E0-I0)        #initial number susceptible
  xstart <- c(time=0, S=S0,
              E1=E10, E2=E20, E3=E30, E4=E40, E5=E50, E6=E60,
              I1=I10, I2=I20, I3=I30, I4=I40, I5=I50, I6=I60,
              R=pop.size-E10-E20-E30-E40-E50-E60-S0-I10-I20-I30-I40-I50-I60) #initial conditions
  data <- vector(mode='list',length=nsims) #initialize list to store the output
  for (k in 1:nsims) {              #simulate nsims times
    data[[k]] <- as.data.frame(model(xstart,params,nstep))
    data[[k]]$cum.time <- cumsum(data[[k]]$time)
  }

  for(i in 1:nsims) data[[i]]$I <- data[[i]]$I1 + data[[i]]$I2 + data[[i]]$I3 + data[[i]]$I4 + data[[i]]

  max.time<-data[[1]]$cum.time[max(which(data[[1]]$I>0))] #maximum time in first simulation
  max.y<-1.8*max(data[[1]]$I)        #find max infected in run 1 and increase by 80% for plot
  plot(I~cum.time,data=data[[1]],xlab='Time (days)',ylab='Cases',col=1,xlim=c(0,max.time),ylim=c(1,max.y
  lines(R~cum.time,data=data[[1]], col=1,xlim=c(0,max.time),ylim=c(0,max.y), lty=1)
  legend('topleft', lty=c(2,1), legend=c('Infectious cases at large','Cumulative reported cases'))
  axis(1, at=seq(0,max.time,5), labels=format(start+seq(0,max.time,5), format= '%b %d'))
  axis(2)
  box()

  for (k in 1:nsims) {              #add multiple epidemics to plot
    lines(I~cum.time,data=data[[k]],col=k,type='l', lty=2)
    lines(R~cum.time,data=data[[k]],col=k, type='l', lty=1)

  }
}

evaluate.model()
```



This model predicts a somewhat faster epidemic growth than observed. This is not surprising since it does not reflect known interventions or the increase in isolation rate that was observed in both SARS and Ebola. Incorportaing a time varying value for γ is the next step with this model.