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Appendix to a review article for The Tokyo Foundation for Policy Research T. Kuniya, K. Shibuya, Y. Tokuda, H. Nakamura, T. Moromizato

1. Simulation results



Figure 1: Time variation of newly reported cases (top) and estimated herd immunity ratio (bottom) for COVID-19 in Japan (2020/1/14 - 2022/3/6).

2. Symbols

Parameter	Description	Value
S	Susceptible population (unvaccinated)	-
E	Exposed population (unvaccinated)	-
Ι	Infectious population (unvaccinated)	-
R	Removed population (unvaccinated)	-
S_1	Susceptible population (vaccinated once)	-
E_1	Exposed population (vaccinated once)	-
I_1	Infectious population (vaccinated once)	-
R_1	Removed population (vaccinated once)	-
S_2	Susceptible population (vaccinated more than twice)	-
E_2	Exposed population (vaccinated more than twice)	-
I_2	Infectious population (vaccinated more than twice)	-
R_2	Removed population (vaccinated more than twice)	-
t	Time	-
a	Class age (time elapsed since the vaccination)	-
β	Infection rate	Estimated using data in [9]
ε	Onset rate	0.2 (incubation period $1/\varepsilon = 5$ days) [4]
γ	Removal rate	0.1 (infection period $1/\gamma = 10$ days) [1]
λ	Force of infection	Equation (1)
$1 - \sigma$	Efficacy of one time vaccination	0.46~[6]
v	Vaccination rate (first)	Estimated using data in [7]
w	Vaccination rate (second)	Estimated using data in [7]
q(a)	Vaccination rate (third) at class age a	Equation (2)
u	Vaccination rate (third)	Estimated using data in [7]
T	Duration between the second and third vaccination	180 days
1-p(a)	Efficacy of full vaccination at class age a	$0.8e^{-0.003a}$ (estimated using data in [6])
δ	Detection rate	0.5 (estimated using data in [5])
N	Total population in Japan	1.26×10^8 [8]

3. Model

Before vaccination (January 14, 2020 - February 16, 2021).

$$S'(t) = -\beta S(t)I(t),$$

$$E'(t) = \beta S(t)I(t) - \varepsilon E(t),$$

$$I'(t) = \varepsilon E(t) - \gamma I(t),$$

$$R'(t) = \gamma I(t).$$

After vaccination (February 17, 2021 - March 6, 2022).

• Unvaccinated population:

$$S'(t) = -\lambda(t)S(t) - vS(t),$$

$$E'(t) = \lambda(t)S(t) - (\varepsilon + v)E(t),$$

$$I'(t) = \varepsilon E(t) - (\gamma + v)I(t),$$

$$R'(t) = \gamma I(t) - vR(t).$$

• Population vaccinated once:

$$S'_{1}(t) = vS(t) - \sigma\lambda(t)S_{1}(t) - wS_{1}(t),$$

$$E'_{1}(t) = vE(t) + \sigma\lambda(t)S_{1}(t) - (\varepsilon + w)E_{1}(t),$$

$$I'_{1}(t) = vI(t) + \varepsilon E_{1}(t) - (\gamma + w)I_{1}(t),$$

$$R'_{1}(t) = vR(t) + \gamma I_{1}(t) - wR_{1}(t).$$

• Population vaccinated more than twice:

$$\begin{split} S_2(t,0) &= wS_1(t) + \int_0^\infty q(a)S_2(t,a)da, \\ &\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right)S_2(t,a) = -p(a)\lambda(t)S_2(t,a) - q(a)S_2(t,a), \\ E_2(t,0) &= wE_1(t) + \int_0^\infty q(a)E_2(t,a)da, \\ &\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right)E_2(t,a) = p(a)\lambda(t)S_2(t,a) - [\varepsilon + q(a)]E_2(t,a), \\ I_2(t,0) &= wI_1(t) + \int_0^\infty q(a)I_2(t,a)da, \\ &\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right)I_2(t,a) = \varepsilon E_2(t,a) - [\gamma + q(a)]I_2(t,a), \\ R_2(t,0) &= wR_1(t) + \int_0^\infty q(a)R_2(t,a)da, \\ &\left(\frac{\partial}{\partial t} + \frac{\partial}{\partial a}\right)R_2(t,a) = \gamma I_2(t,a) - q(a)R_2(t,a). \\ & 3 \end{split}$$

• Force of infection:

$$\lambda(t) = \beta \left[I(t) + I_1(t) + \int_0^\infty I_2(t, a) da \right].$$
(1)

• Vaccination rate (third) at time *a* passed since the second vaccination:

$$q(a) = \begin{cases} 0, & a < T, \\ u, & \text{otherwise.} \end{cases}$$
(2)

• Efficacy of full vaccination at class age $a: 1 - p(a) = 0.8e^{-0.003a}$, which is fitted to the data in [6] as shown in Figure 2.





- Full immunity at time t: $1 S(t) S_1(t) \int_0^\infty S_2(t, a) da$.
- Partial immunity at time t: 1 S(t).

How to estimate $\beta = \beta(t)$

Let the unit time be 1 day. Newly reported cases per day: let A(t) be the actual data collected from [9] and let

$$\begin{aligned} Y(t) &:= (\text{detection rate } \delta) \\ &\times (\text{newly removed } \gamma \left[I(t) + I_1(t) + \int_0^\infty I_2(t, a) da \right]) \\ &\times (\text{total population } N), \end{aligned}$$

be the simulation data. For $t \leq 7$, we assume $\beta = 0.25$ so that the basic reproduction number $\mathcal{R}_0 = \beta/\gamma = 2.5$ [2]. For t > 7 ($t \in \mathbb{Z}$), we seek $\beta = \beta^*$ that minimizes the least square error

$$L(\beta) := \sum_{s=1}^{7} [Y(t-s) - A(t-s)]^2$$

and let $\beta(t) = \beta^*$. In other words, we repeatedly estimate $\beta(t)$ using data in previous 1 week. Simulation is carried out using the above model with initial condition

$$Y(0) = 1$$
, $I(0) = \frac{Y(0)}{\delta \gamma N}$, $S(0) = 1 - I(0)$,

and other variables are zero.

How to estimate v, w and u

Note that $v \times [S(t) + E(t) + I(t) + R(t)] \times N$ is the number of first vaccination at time t. Hence, we estimate v = v(t) as

$$v(t) = \frac{(number \ of \ first \ vaccination \ at \ time \ t \ [7])}{[S(t) + E(t) + I(t) + R(t)] \times N}.$$

In a similar manner, we estimate w = w(t) and u = u(t) as

$$w(t) = \frac{(number \ of \ second \ vaccination \ at \ time \ t \ [7])}{[S_1(t) + E_1(t) + I_1(t) + R_1(t)] \times N},$$

and

$$u(t) = \frac{(number \ of \ third \ vaccination \ at \ time \ t \ [7])}{\int_T^\infty [S_2(t,a) + E_2(t,a) + I_2(t,a) + R_2(t,a)] da \times N},$$

respectively.

How to estimate δ

To estimate δ , we used the data in [5]. Taking average of each data in [5], we obtain the herd immunity ratio at June 2020 as 0.1%; at December 2020 as 0.662%; at December 2021 as 2.158%. We estimated $\delta = 0.5$ by fitting the curve to the data as shown in Figure 3.



Figure 3: Time variation of herd immunity ratio for COVID-19 in Japan (2020/1/14 - 2022/3/6).

4. Limitations

The following factors are not explicitly considered in our model.

- 1. Seasonality;
- 2. Virus mutation;
- 3. Behavior change;
- 4. Different susceptibility;
- 5. Space structure;
- 6. (Chronological) age structure;
- 7. Stochasticity.

Since we estimated β for each day, effects of 1-3 on the infection rate may be implicitly considered in our model. However, effect of 2 on the herd immunity is not considered and this may lead to the overestimation of the herd immunity. On the other hand, considering 4 may decrease the critical proportion of immunization [3]. Considering 5-7 could improve the model but the estimation may become more complex.

References

- R.M. Anderson, H. Heesterbeek, D. Klinkenberg, T.D. Hollingsworth, How will country-based mitigation measures influence the course of the COVID-19 epidemic?, The Lancet 395 (2020) 21–27.
- N. Imai, A. Cori, I. Dorigatti, et al., Report 3: Transmissibility of 2019-nCoV (2020). https://www. imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-01-25-COVID19-Report-3. pdf, accessed on March 8, 2022.
- [3] 稲葉寿, 感染症数理モデルと COVID-19, https://www.covid19-jma-medical-expert-meeting.jp/ topic/3925, accessed on March 8, 2022.
- [4] N.M. Linton, T. Kobayashi, Y. Yang, et al., Incubation period and other epidemiological characteristics of 2019 novel coronavirus infections with right truncation: a statistical analysis of publicly available case data, J. Clin. Med. 9 (2020) 538.
- [5] m3.com, 自然感染による抗体保有率、東京 2.80%・大阪 3.78%に, https://www.m3.com/news/open/ iryoishin/1017268, accessed on March 8, 2022.
- [6] NIID 国立感染症研究所,新型コロナワクチンの有効性を検討した症例対照研究の暫定報告(第三報), https: //www.niid.go.jp/niid/ja/2019-ncov/2484-idsc/10966-covid19-71.html, accessed on March 7, 2022.
- [7] Prime Minister of Japan and His Cabinet, https://www.kantei.go.jp/jp/headline/kansensho/ vaccine.html, accessed on March 8, 2022.
- [8] Statistics Bureau Japan, Population estimates monthly report, https://www.stat.go.jp/english/ data/jinsui/tsuki/index.html, accessed on March 7, 2022.
- [9] WHO Coronavirus (COVID-19) Dashboard, https://covid19.who.int/, accessed on March 8, 2022.

MATLAB code for main simulation

- 'cases.xlsx' is an excel file collecting the newly reported cases of COVID-19 per day in Japan from 2020/1/14 to 2022/3/6.
- 'vaccine.xlsx' is an excel file collecting the newly number of vaccination against COVID-19 per day in Japan from 2020/1/14 to 2022/3/6.

```
1 clear
 2 tic
3
4 A=xlsread('cases.xlsx');
5 B=xlsread('vaccine.xlsx');
 6
7 gam=1/10;
 8 eps=1/5;
9 N=1.26*10^8;
10 del=0.5;
11 sig=0.54;
^{12}
13 pp=0.003;
14
15 dt=1;te=max(size(A))-1;nt=te/dt;
16 T=180;nT=T/dt;
17 da=1;ae=4*T;na=ae/da;
18
19 Y(1)=1;
20 I(1)=Y(1)/(del*N*gam);
21 S(1)=1-I(1);
22 E(1)=0;
23 R(1)=0;
24 S1(1)=0;
25 E1(1)=0;
26 I1(1)=0;
27 R1(1)=0;
^{28}
29 for a=1:1:na
30
       S2(1,a)=0;
       E2(1,a)=0;
31
       I2(1,a)=0;
32
33
       R2(1,a)=0;
34 end
35 SS(1) = sum(S2(1,1:1:na)) * da;
36 EE(1)=sum(E2(1,1:1:na))*da;
37 II(1)=sum(I2(1,1:1:na))*da;
38 RR(1) = sum(R2(1,1:1:na)) * da;
39
40 db=0.01; be=4; nb=be/db;
^{41}
42 t0=7/dt;
43 t1=401/dt; %2021/2/17 start of vaccination
^{44}
45 for t=1:1:nt
      if B(round(t*dt), 2) == 0
46
47
           v(t)=0;
       end
^{48}
```

```
if B(round(t*dt), 3) == 0
 49
              w(t) = 0;
 50
 51
         end
         if B(round(t*dt), 4) == 0
 52
 53
             u(t)=0;
 54
         end
 55
         if t < t0
 56
 57
              bet=0.25;
              S(t+1) = S(t) + dt * (-bet * S(t) * I(t));
 58
 59
              E(t+1) = E(t) + dt * (bet * S(t) * I(t) - eps * E(t));
              I(t+1) = I(t) + dt * (eps * E(t) - gam * I(t));
 60
              R(t+1) = R(t) + dt * qam * I(t);
 61
              Y(t+1)=del*N*gam*I(t+1);
 62
              S1(t+1)=0;
 63
              E1(t+1)=0;
 64
              I1(t+1)=0;
 65
              R1(t+1)=0;
 66
 \mathbf{67}
              for a=1:1:na
                   S2(t+1, a) = 0;
 68
                   E2(t+1, a) = 0;
 69
 70
                   I2(t+1, a) = 0;
                   R2(t+1, a) = 0;
 71
 72
              end
         elseif t<t1
 73
              for b=1:1:nb
 74
 75
                  bet=b*db;
 76
                   for s=1:1:t0
                      S(t+s-t0+1) = S(t+s-t0) + dt * (-bet * S(t+s-t0) * I(t+s-t0));
 77
 78
                      E(t+s-t0+1) = E(t+s-t0) + dt * (bet * S(t+s-t0) * I(t+s-t0) ...
                           -eps*E(t+s-t0));
 79
                      I(t+s-t0+1)=I(t+s-t0)+dt*(eps*E(t+s-t0)-gam*I(t+s-t0));
 80
 81
                      R(t+s-t0+1) = R(t+s-t0) + dt + gam + I(t+s-t0);
                      Y(t+s-t0+1) = del *N*gam*I(t+s-t0+1);
 82
                      Z(t+s-t0+1) = (Y(t+s-t0+1) - A(round((t+s-t0+1)*dt), 1))^2;
 83
                   end
 84
                   L(b) = sum(Z(t-t0+2:1:t+1));
 85
 86
              end
              [L1 L2]=min(L);
 87
              bet=L2*db;
 88
 89
              for s=1:1:t0+1
 90
                   S(t+s-t0+1) = S(t+s-t0) + dt * (-bet * S(t+s-t0) * I(t+s-t0));
 91
 92
                   E(t+s-t0+1) = E(t+s-t0) + dt * (bet * S(t+s-t0) * I(t+s-t0) ...
                       -eps*E(t+s-t0));
93
                   I(t+s-t0+1)=I(t+s-t0)+dt*(eps*E(t+s-t0)-gam*I(t+s-t0));
 ^{94}
                   R(t+s-t0+1) = R(t+s-t0) + dt * gam * I(t+s-t0);
 95
                   Y(t+s-t0+1)=del*N*gam*I(t+s-t0+1);
96
                   S1(t+s-t0+1)=0;
 97
                   E1(t+s-t0+1)=0;
 98
                   I1(t+s-t0+1)=0;
99
                   R1 (t+s-t0+1) = 0;
100
                   for a=1:1:na
101
102
                       S2(t+s-t0+1,a)=0;
                        E2(t+s-t0+1,a)=0;
103
                       I2(t+s-t0+1,a)=0;
104
105
                       R2(t+s-t0+1,a)=0;
                   end
106
                   SS(t+s-t0+1)=sum(S2(t+s-t0+1,1:1:na))*da;
107
```

```
EE(t+s-t0+1) = sum(E2(t+s-t0+1,1:1:na))*da;
108
                  II(t+s-t0+1) = sum(I2(t+s-t0+1,1:1:na)) * da;
109
110
                  RR(t+s-t0+1)=sum(R2(t+s-t0+1,1:1:na))*da;
111
             end
         else
112
113
             for b=1:1:nb
                  bet=b*db;
114
115
                  for s=1:1:t0
116
                       if B(round((t+s-t0)*dt), 2) \neq 0
                           v(t+s-t0) = B(round((t+s-t0)*dt), 2)/((S(t+s-t0)...)
117
118
                                +E(t+s-t0)+I(t+s-t0)+R(t+s-t0))*N);
119
                       else
                           v(t+s-t0) = 0;
120
                       end
121
                       if B(round((t+s-t0)*dt), 3) \neq 0
122
                           w(t+s-t0) = B(round((t+s-t0)*dt), 3) / ((S1(t+s-t0)...)
123
                                +E1(t+s-t0)+I1(t+s-t0)+R1(t+s-t0))*N);
124
125
                      else
126
                           w(t+s-t0)=0;
                       end
127
                       if B(round((t+s-t0)*dt), 4) \neq 0
128
129
                           u(t+s-t0) = B(round((t+s-t0)*dt), 4)/...
                                ((sum(S2(t+s-t0,nT:1:na))+sum(E2(t+s-t0,nT:1:na))...
130
131
                                +sum(I2(t+s-t0,nT:1:na))...
                                +sum(R2(t+s-t0,nT:1:na)))*da*N);
132
133
                       else
134
                           u(t+s-t0)=0;
135
                       end
136
137
                      QS=u(t+s-t0) * sum(S2(t+s-t0,nT:1:na-1)) * da;
                       QE=u(t+s-t0) * sum(E2(t+s-t0,nT:1:na-1)) * da;
138
                      OI=u(t+s-t0)*sum(I2(t+s-t0,nT:1:na-1))*da;
139
140
                       QR=u(t+s-t0)*sum(R2(t+s-t0,nT:1:na-1))*da;
141
142
                      lam(t+s-t0) = bet * (I(t+s-t0)+I1(t+s-t0)...
                           +sum(I2(t+s-t0,1:1:na))*da);
143
144
145
                      S(t+s-t0+1) = S(t+s-t0) + dt * (-lam(t+s-t0) * S(t+s-t0) ...
                           -v(t+s-t0)*S(t+s-t0));
146
                      E(t+s-t0+1) = E(t+s-t0) + dt * (lam(t+s-t0) * S(t+s-t0) ...
147
148
                            -(eps+v(t+s-t0))*E(t+s-t0));
                       I(t+s-t0+1) = I(t+s-t0) + dt * (eps * E(t+s-t0) ...
149
150
                           -(gam+v(t+s-t0))*I(t+s-t0));
                      R(t+s-t0+1) = R(t+s-t0) + dt * (gam * I(t+s-t0)...
151
                           -v(t+s-t0) * R(t+s-t0));
152
153
154
                      S1(t+s-t0+1) = S1(t+s-t0) + dt * (v(t+s-t0) * S(t+s-t0) ...
                           -sig*lam(t+s-t0)*S1(t+s-t0)-w(t+s-t0)*S1(t+s-t0));
155
                       E1(t+s-t0+1)=E1(t+s-t0)+dt*(v(t+s-t0)*E(t+s-t0)..
156
                           +sig*lam(t+s-t0)*S1(t+s-t0)-(eps+w(t+s-t0))*E1(t+s-t0));
157
158
                       I1(t+s-t0+1) = I1(t+s-t0) + dt * (v(t+s-t0) * I(t+s-t0) ...
                           +eps*E1(t+s-t0)-(gam+w(t+s-t0))*I1(t+s-t0));
159
                      R1(t+s-t0+1) = R1(t+s-t0) + dt * (v(t+s-t0) * R(t+s-t0) ...
160
161
                           +gam*I1(t+s-t0)-w(t+s-t0)*R1(t+s-t0));
162
163
                      S2(t+s-t0+1, 1) = w(t+s-t0) * S1(t+s-t0) + OS;
                       E2(t+s-t0+1, 1) = w(t+s-t0) * E1(t+s-t0) + QE;
164
                      I2(t+s-t0+1,1) = w(t+s-t0) * I1(t+s-t0) + QI;
165
166
                      R2(t+s-t0+1, 1) = w(t+s-t0) * R1(t+s-t0) + OR;
```

167	<pre>for a=2:1:nT</pre>
168	S2(t+s-t0+1,a)=S2(t+s-t0,a)+dt*(-(S2(t+s-t0,a)
169	-S2(t+s-t0,a-1))/da
170	-p(pp,(a-1)*da)*lam(t+s-t0)*S2(t+s-t0,a-1));
171	E2(t+s-t0+1,a)=E2(t+s-t0,a)+dt*(-(E2(t+s-t0,a)
172	-E2(t+s-t0,a-1))/da
173	+p(pp, (a-1)*da)*lam(t+s-t0)*S2(t+s-t0, a-1)
174	$-eps \star E2(t+s-t0, a-1));$
175	12(t+s-t0+1,a) = 12(t+s-t0,a) + dt * (-(12(t+s-t0,a))
176	-12(t+s-t0,a-1))/da
177	Teps*E2(l+s-l0, d-1) - gdll*12(l+s-l0, d-1)); P2(l+s-l0+1, z) - P2(l+s-l0, z) + dt + (-(P2(l+s-l0, z)));
178	$\frac{-P^{2}(t+s-t)}{-P^{2}(t+s-t)} = \frac{-P^{2}(t+s-t)}{-P^{2}(t+s-t)} = -P$
180	end
181	for a=nT+1:1:na
182	S2(t+s-t0+1,a) = S2(t+s-t0,a) + dt * (-(S2(t+s-t0,a))
183	-S2(t+s-t0,a-1))/da
184	-p(pp, (a-1)*da)*lam(t+s-t0)*S2(t+s-t0, a-1)
185	-u(t+s-t0)*S2(t+s-t0,a-1));
186	E2(t+s-t0+1,a)=E2(t+s-t0,a)+dt*(-(E2(t+s-t0,a)
187	-E2(t+s-t0,a-1))/da
188	+p(pp,(a-1)*da)*lam(t+s-t0)*S2(t+s-t0,a-1)
189	<pre>-eps*E2(t+s-t0,a-1)-u(t+s-t0)*E2(t+s-t0,a-1));</pre>
190	I2(t+s-t0+1,a) = I2(t+s-t0,a) + dt * (-(I2(t+s-t0,a))
191	-I2(t+s-t0,a-1))/da
192	$+eps \star E2(t+s-t0, a-1) - gam \star I2(t+s-t0, a-1) \dots$
193	-u(t+s-t0)*12(t+s-t0,a-1));
194	RZ(t+s-t0+1,a) = RZ(t+s-t0,a) + at * (-(RZ(t+s-t0,a))
195	-RZ(l+S-l0, d-1))/dd
195	end
198	
199	Y(t+s-t0+1)=del*N*gam*(I(t+s-t0+1)+I1(t+s-t0+1)
200	+sum(I2(t+s-t0+1,1:1:na))*da);
201	$Z(t+s-t0+1) = (Y(t+s-t0+1) - A(round((t+s-t0+1)*dt), 1))^2;$
202	end
203	L(b) = sum(Z(t-t0+2:1:t+1));
204	end
205	[L1 L2]=min(L);
206	<pre>bet=L2*db;</pre>
207	
208	for s=1:1:t0+1
209	$II B(round((t+s-t0) * dt), 2) \neq 0$
210	V(l+S-L0) = B(round((l+S-L0)*dL), 2) / ((S(l+S-L0)+E(l+S-L0))
211	+1(t+S-t0)+K(t+S-t0)/K(;
212	(1 + c - t 0) = 0
214	end
215	if B(round((t+s-t0)*dt).3) $\neq 0$
216	w(t+s-t0) = B(round((t+s-t0)*dt), 3)/((S1(t+s-t0)+E1(t+s-t0))
217	+I1(t+s-t0)+R1(t+s-t0))*N;
218	else
219	w(t+s-t0)=0;
220	end
221	if $B(round((t+s-t0)*dt), 4) \neq 0$
222	u(t+s-t0)=B(round((t+s-t0)*dt),4)/
223	((sum(S2(t+s-t0,nT:1:na))+sum(E2(t+s-t0,nT:1:na))
224	+sum(I2(t+s-t0,nT:1:na))+sum(R2(t+s-t0,nT:1:na)))*da*N);
225	else

226	u(t+s-t0)=0;
227	end
228	
229	<pre>QS=u(t+s-t0)*sum(S2(t+s-t0,nT:1:na-1))*da;</pre>
230	<pre>QE=u(t+s-t0)*sum(E2(t+s-t0,nT:1:na-1))*da;</pre>
231	QI=u(t+s-t0)*sum(I2(t+s-t0,nT:1:na-1))*da;
232	<pre>QR=u(t+s-t0)*sum(R2(t+s-t0,nT:1:na-1))*da;</pre>
233	
234	lam(t+s-t0)=bet*(I(t+s-t0)+I1(t+s-t0)+sum(I2(t+s-t0,1:1:na))*da);
235	
236	S(t+s-t0+1) = S(t+s-t0) + dt * (-lam(t+s-t0) * S(t+s-t0)
237	-v(t+s-t0)*S(t+s-t0));
238	E(t+s-t0+1)=E(t+s-t0)+dt*(lam(t+s-t0)*S(t+s-t0)
239	-(eps+v(t+s-t0))*E(t+s-t0));
240	I(t+s-t0+1) = I(t+s-t0) + dt * (eps * E(t+s-t0)
241	-(qam+v(t+s-t0))*I(t+s-t0));
242	R(t+s-t0+1) = R(t+s-t0) + dt * (gam * I(t+s-t0) - v(t+s-t0) * R(t+s-t0));
243	
244	S1(t+s-t0+1)=S1(t+s-t0)+dt*(v(t+s-t0)*S(t+s-t0)
245	-sig*lam(t+s-t0)*S1(t+s-t0)-w(t+s-t0)*S1(t+s-t0));
246	E1(t+s-t0+1)=E1(t+s-t0)+dt*(v(t+s-t0)*E(t+s-t0)
247	+sig*lam(t+s-t0)*S1(t+s-t0)-(eps+w(t+s-t0))*E1(t+s-t0));
248	I1(t+s-t0+1)=I1(t+s-t0)+dt*(v(t+s-t0)*I(t+s-t0)
249	$+eps \times E1(t+s-t0) - (gam + w(t+s-t0)) \times I1(t+s-t0));$
250	R1(t+s-t0+1) = R1(t+s-t0) + dt * (v(t+s-t0) * R(t+s-t0))
251	+gam*I1(t+s-t0)-w(t+s-t0)*R1(t+s-t0));
252	J. (, (, (,,,,,
253	S2(t+s-t0+1,1) = w(t+s-t0) * S1(t+s-t0) + OS;
254	E2(t+s-t0+1,1) = w(t+s-t0) * E1(t+s-t0) + OE;
255	I2(t+s-t0+1,1) = w(t+s-t0) * I1(t+s-t0) + 0I;
256	R2(t+s-t0+1, 1) = w(t+s-t0) * R1(t+s-t0) + OR;
257	for a=2:1:nT
258	S2(t+s-t0+1,a) = S2(t+s-t0,a)+dt*(-(S2(t+s-t0,a))
259	-S2(t+s-t0,a-1))/da
260	-p(pp, (a-1)*da)*lam(t+s-t0)*S2(t+s-t0, a-1));
261	E2(t+s-t0+1,a) = E2(t+s-t0,a) + dt + (-(E2(t+s-t0,a))
262	-E2(t+s-t0,a-1))/da
263	+p(pp, (a-1)*da)*lam(t+s-t0)*S2(t+s-t0, a-1)
264	$-eps \times E2(t+s-t0, a-1));$
265	I2(t+s-t0+1,a) = I2(t+s-t0,a) + dt * (-(I2(t+s-t0,a))
266	-I2(t+s-t0,a-1))/da
267	$+eps \times E2(t+s-t0, a-1) - gam \times I2(t+s-t0, a-1));$
268	R2(t+s-t0+1,a) = R2(t+s-t0,a) + dt * (-(R2(t+s-t0,a))
269	-R2(t+s-t0,a-1))/da+gam*I2(t+s-t0,a-1));
270	end
271	<pre>for a=nT+1:1:na</pre>
272	S2(t+s-t0+1,a)=S2(t+s-t0,a)+dt*(-(S2(t+s-t0,a)
273	-S2(t+s-t0,a-1))/da
274	-p(pp, (a-1)*da)*lam(t+s-t0)*S2(t+s-t0, a-1)
275	-u(t+s-t0)*S2(t+s-t0,a-1));
276	E2(t+s-t0+1,a)=E2(t+s-t0,a)+dt*(-(E2(t+s-t0,a)
277	-E2(t+s-t0,a-1))/da
278	+p(pp, (a-1)*da)*lam(t+s-t0)*S2(t+s-t0, a-1)
279	$-eps \times E2(t+s-t0, a-1) - u(t+s-t0) \times E2(t+s-t0, a-1));$
280	I2(t+s-t0+1,a)=I2(t+s-t0,a)+dt*(-(I2(t+s-t0,a))
281	-I2(t+s-t0,a-1))/da+eps+E2(t+s-t0,a-1)
282	$-qam \times I2(t+s-t0,a-1)-u(t+s-t0) \times I2(t+s-t0,a-1));$
283	R2(t+s-t0+1,a) = R2(t+s-t0,a)+dt * (-(R2(t+s-t0,a))
284	-R2(t+s-t0,a-1))/da
1	

```
285
                         +gam*I2(t+s-t0,a-1)-u(t+s-t0)*R2(t+s-t0,a-1));
286
                 end
287
288
                 Y(t+s-t0+1)=del*N*gam*(I(t+s-t0+1)+I1(t+s-t0+1)...
                    +sum(I2(t+s-t0+1,1:1:na))*da);
289
                 SS(t+s-t0+1)=sum(S2(t+s-t0+1,1:1:na))*da;
290
                 EE(t+s-t0+1) = sum(E2(t+s-t0+1,1:1:na)) * da;
291
                 II(t+s-t0+1) = sum(I2(t+s-t0+1,1:1:na))*da;
292
293
                 RR(t+s-t0+1)=sum(R2(t+s-t0+1,1:1:na))*da;
            end
294
        end
295
296 end
297
298 T1=1:1:nt*dt;
299 T2=1:1:nt-1;
300 plot(T1,A(T1,1),'o',T2*dt,Y(T2),'-','Markersize',1.5,'Linewidth',2)
301 newcolors = {'#D95319','#0072BD'};
302 colororder(newcolors)
303 toc
```