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A DAE Approach to Control SEIR-ODEs

Ein DAE Ansatz zur Kontrolle von SEIR-Differentialgleichungen (englischsprachig)

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A DAE Approach to Control SEIR-ODEs

Diana Estévez Schwarz

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Abstract

For the current COVID-19 pandemic, well-founded strategies to cope with the dynamics of the epidemic are urgently needed. Reading [1]-[2] and reflecting about higher-index DAEs resulting from control problems, the author wondered whether this point of view could provide some new insights for a better understanding of the SEIR-ODEs and at last, for the design of infection regulating policies. Indeed, the obtained mathematical results seem to be very plausible and deliver a simple theoretical rule of thumb to estimate a reproduction number that avoids dangerous peaks in the infected population. A corresponding simple control strategy for the SEIR-ODE has been implemented in Python and provides numerical solutions for a non-increasing infected population.

1 Introduction

1.1 The SEIR Model

The ordinary differential equation (ODE) corresponding to the classical infectious disease model SEIR (Susceptible $\rightarrow$ Exposed $\rightarrow$ Infected $\rightarrow$ Removed) with the notation used in [2] reads:

$$S' = -\frac{\mathcal{R}_t}{T_{inf}} \cdot I \cdot S, \tag{1}$$

$$E' = \frac{\mathcal{R}_t}{T_{inf}} \cdot I \cdot S - \frac{1}{T_{inc}} \cdot E, \tag{2}$$

$$I' = \frac{1}{T_{inc}} \cdot E - \frac{1}{T_{inf}} \cdot I, \tag{3}$$

$$R' = \frac{1}{T_{inf}} \cdot I. \tag{4}$$

The considered period parameters (in days) are:

- T_{inc}: Length of incubation period
- T_{inf}: Duration patient is infectious

The reproduction number or measure of contagiousness $\mathcal{R}_t$ is the number of secondary infections each infected individual produces. We consider:

- a constant $\mathcal{R}_t = \mathcal{R}_0$ for a constant basic reproduction number,

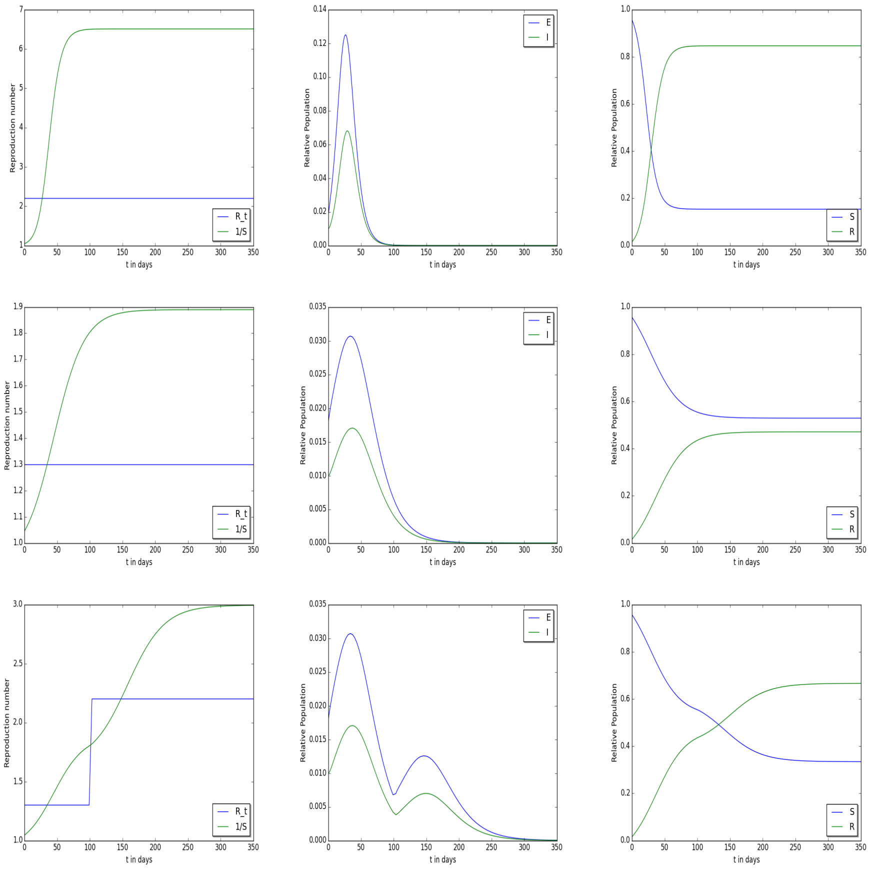

Figure 1: Some results for a $\mathcal{R}_t = 2.2$ (top),$\mathcal{R}_t = 1.3$ and a step-wise defined $\mathcal{R}_t$ (bottom) function i. In the left images we included the estimate $\frac{1}{S}$, cf. Section 1.2. Please notice the different scalings.

- a constant $\mathcal{R}_t < \mathcal{R}_0$ decreased reproduction number that may result from specific policies such as social distancing,
- a time-dependent $\mathcal{R}_t(t)$.

For given positive initial values S_0, E_0, I_0, R_0 fulfilling

$$S_0 + E_0 + I_0 + R_0 = 1$$

the solution of the SEIR-ODE can be computed for constant or time-dependent $\mathcal{R}_t(t)$. In Figure 1 we present some examples for $T_{inc} = 5.20$ and $T_{inf} = 2.9$, the default parameters in [2].

In this article, we focus on the estimation of an appropriate $\mathcal{R}_t(t)$ allowing the healthcare system to cope with the corresponding infected population $I(t)$, cf. [1].

This problem seems to be analogous to tracking problems. Therefore, in the following we investigate its mathematical properties from a DAE (differential-algebraic equation) point of view. The obtained results match the expectations.

1.2 Results and Plausible Conclusion

In Sections 2-4, we will compute explicit solutions for $\mathcal{R}_t, S, E, R$ if $I = i(t)$ is prescribed to keep the infectious population at or under a certain level. Moreover, from our analysis and tests we confirmed that a plausible rule of thumb to estimate $\mathcal{R}_t$ such that for an affordable I_0 also I remains affordable is

$$\mathcal{R}_t(t) \leq \min\left\{\mathcal{R}_0, \frac{1}{S}\right\}.$$

This implies that estimations of the susceptible population are crucial for reviewing the need for restrictions.

Interpreting this results in terms of the equation (2)-(3) is quite simple:

- To ensure $I' \leq 0$ according to (3)

  $$\frac{1}{T_{inc}} \cdot E \leq \frac{1}{T_{inf}} \cdot I$$

  has to be given.

- If the last inequality is given and $\mathcal{R}_t(t) \leq \frac{1}{S}$, then from (2) we obtain

  $$E' \leq \frac{\mathcal{R}_t}{T_{inf}} \cdot I \cdot S - \frac{1}{T_{inf}} \cdot I \leq 0.$$

With these properties in mind, in Section 5 we provide a corresponding strategy for controlling $\mathcal{R}_t$ directly in the ODE (1)-(4) that has been implemented in Python and can be used for further numerical experiments.

2 DAE-Formulation

Let us consider

1. the SEIR-ODE with an unknown function $\mathcal{R}_t(t)$,
2. a constraint that prescribes the percentage of the infected population I,

leading to the differential-algebraic equation (DAE)

$$\begin{aligned}
S' &= -\frac{\mathcal{R}_t}{T_{inf}} \cdot I \cdot S, && (5)\\
E' &= \frac{\mathcal{R}_t}{T_{inf}} \cdot I \cdot S - \frac{1}{T_{inc}} \cdot E, && (6)\\
I' &= \frac{1}{T_{inc}} \cdot E - \frac{1}{T_{inf}} \cdot I, && (7)\\
R' &= \frac{1}{T_{inf}} \cdot I, && (8)\\
0 &= I - i(t). && (9)
\end{aligned}$$

In the DAE, the reproduction number $\mathcal{R}_t(t)$ is an unknown function that will be computed in dependence of the parameters, the initial values and a given time-dependent function $i(t)$.

From a DAE point of view, (5)-(9) is an index-3 DAE with the following constraints:

1. We have the explicit contraint (9):
$$I = i(t). \tag{10}$$

2. The differentiation of (10) together with (7) leads to
$$i'(t) \quad = \quad \frac{1}{T_{inc}} \cdot E - \frac{1}{T_{inf}} \cdot i(t),$$
and therefore to the constraint
$$E = T_{inc}\left(i'(t) + \frac{1}{T_{inf}} \cdot i(t)\right). \tag{11}$$

3. Differentiating (11) we obtain
$$E' = T_{inc}\left(i''(t) + \frac{1}{T_{inf}} \cdot i'(t)\right),$$
and, using (6), therefore
$$\frac{\mathcal{R}_t}{T_{inf}} \cdot I \cdot S - \frac{1}{T_{inc}} \cdot E \quad = \quad T_{inc}\left(i''(t) + \frac{1}{T_{inf}} \cdot i'(t)\right),$$
such that we obtain the constraint
$$\frac{\mathcal{R}_t}{T_{inf}} \cdot i(t) \cdot S - \left(i'(t) + \frac{1}{T_{inf}} \cdot i(t)\right) \quad = \quad T_{inc}\left(i''(t) + \frac{1}{T_{inf}} \cdot i'(t)\right), \tag{12}$$
or, more precisely,

$$\mathcal{R}_t \cdot S = \frac{T_{inf}}{i(t)}\left(\left(i'(t) + \frac{1}{T_{inf}} \cdot i(t)\right) + \ T_{inc}\left(i''(t) + \frac{1}{T_{inf}} \cdot i'(t)\right)\right) =: r(t). \tag{13}$$

In practice $\mathcal{R}_t$ will not be larger than the basic reproduction number $\mathcal{R}_0$. Hence, we consider the constraint
$$\mathcal{R}_t = \min\left\{\mathcal{R}_0, \frac{r(t)}{S}\right\}. \tag{14}$$

We emphasize that $r(t)$ depends on $i(t), i'(t)$ and $i''(t)$, because the DAE-index was 3. For the function $i(t)$ we will investigate the following special cases:

1. If $i(t) = I_0$ is constant, then $r(t) = 1$ and
$$\mathcal{R}_t = \min\left\{\mathcal{R}_0, \frac{1}{S}\right\}.$$

2. If $i(t) = I_0\ \mathrm{e}^{-\frac{t}{T_{inf}}}$ or $i(t) = I_0\ \mathrm{e}^{-\frac{t}{T_{inc}}}$, then

$$\mathcal{R}_t \cdot S = 0,$$

i.e. $\mathcal{R}_t$ should be zero since we assume $S \neq 0$.

3. If

$$i(t) = I_0\ \mathrm{e}^{-\lambda\ t},$$

then we have

$$i'(t) = -\lambda\ i(t), \quad i''(t) = -\lambda i'(t) = \lambda^2 i(t)$$

and therefore for all t:

$$r(\lambda) \quad = \quad (T_{\text{inc}}\,\lambda - 1)\ (T_{\text{inf}}\,\lambda - 1)\,.$$

4. For our tests, we will also consider an oscillating $i(t)$ of the form

$$i(t) = I_0\,(1 + a\ \sin(b\ t))\,.$$

3 Solving an Associated ODE

Due to the constraints (10),(11),(13), the solution of the index-3 DAE (5) -(9) for a given $i(t)$ can be computed as follows:

1. Compute I and E according to (10),(11). Note that I_0 and E_0 are fixed by the contraints at t_0.

2. Consider initial values S_0 and R_0 at t_0 fulfilling $S_0 + R_0 + I_0 + E_0 = 1$ and solve the ODE

$$S' \quad = \quad -g(t), \tag{15}$$

$$R' \quad = \quad \frac{1}{T_{inf}} \cdot i(t), \tag{16}$$

for

$$g(t) := \left(i'(t) + \frac{1}{T_{inf}} \cdot i(t)\right) +\ T_{inc}\left(i''(t) + \frac{1}{T_{inf}} \cdot i'(t)\right) = \frac{i(t)}{T_{inf}} r(t).$$

Since the right-hand side depends on t only, the solution can be obtained by integration:

$$S \quad = \quad S_0\ - \int_{t_0}^{t} g(\tau)\ d\tau, \tag{17}$$

$$R \quad = \quad R_0 + \int_{t_0}^{t} \frac{1}{T_{inf}} \cdot i(\tau)\ d\tau. \tag{18}$$

3. $\mathcal{R}_t$ results from

$$\mathcal{R}_t = \frac{r(t)}{S} = \frac{r(t)}{S_0 - \int_{t_0}^{t} g(\tau)\ d\tau}. \tag{19}$$

Note that this result permits an simple representation of the solution if we assume that i is an exponential function of the form:

$$i(t) = I_0 \mathrm{e}^{-\lambda t}.$$

In this case, equations (11), (17), (19) for $t_0 = 0$ lead to

$$\begin{aligned}
E(t) &= -\frac{T_{\mathrm{inc}}}{T_{\mathrm{inf}}} \left(T_{\mathrm{inf}}\ \lambda - 1\right) i(t), && (20)\\
S(t) &= S_0 - \frac{r(\lambda)}{T_{\mathrm{inf}}\ \lambda} \left(I_0 - i(t)\right), && (21)\\
R(t) &= R_0 + \frac{1}{T_{\mathrm{inf}}\ \lambda} \left(I_0 - i(t)\right), && (22)\\
\mathcal{R}_t(t) &= \frac{r(\lambda)}{S_0 - \frac{r(\lambda)}{T_{\mathrm{inf}}\ \lambda} \left(I_0 - i(t)\right)}. && (23)
\end{aligned}$$

4 Some Tests for the DAE-Formulation

We tested the following cases for $T_{inc} = 5.20$ and $T_{inf} = 2.9$:

1. $i(t) = I_0 = 0.01$,
2. $i(t) = 0.01\mathrm{e}^{-\frac{0.01}{T_{inf}}t}$,
3. $i(t) = 0.01\left(1. + 0.05 \sin\left(\frac{2\pi}{21}t\right)\right)$. We considered the period 21 days inspired by regulations of the British government[1].

The results can be found in Figure 2. For the numerical solution, the algorithms described in [3] were used. However, the explicit formulas developed above could also have been used.

For the considered parameters, the results can be interpreted as follows:

1. $i(t) = I_0 = 0.01$ is theoretically possible and easy to estimate,
2. a moderately exponentially decreasing $i(t)$ postpones the time-point at witch social distancing can end, i.e. $\mathcal{R}_t = \mathcal{R}_0$,
3. an oscillating $i(t)$ requires a considerably oscillating $\mathcal{R}_t$, whereas the overall behavior of S and R results to be similar as for $i(t) = I_0 = 0.01$.

All in all, we recognize that reducing the social distancing measures such that for $\mathcal{R}_t$

$$\mathcal{R}_t \leq \min\left\{\mathcal{R}_0, \frac{1}{S}\right\}$$

is always given seems to be a desirable goal.

[1] `https://www.legislation.gov.uk/uksi/2020/350/regulation/3/made`

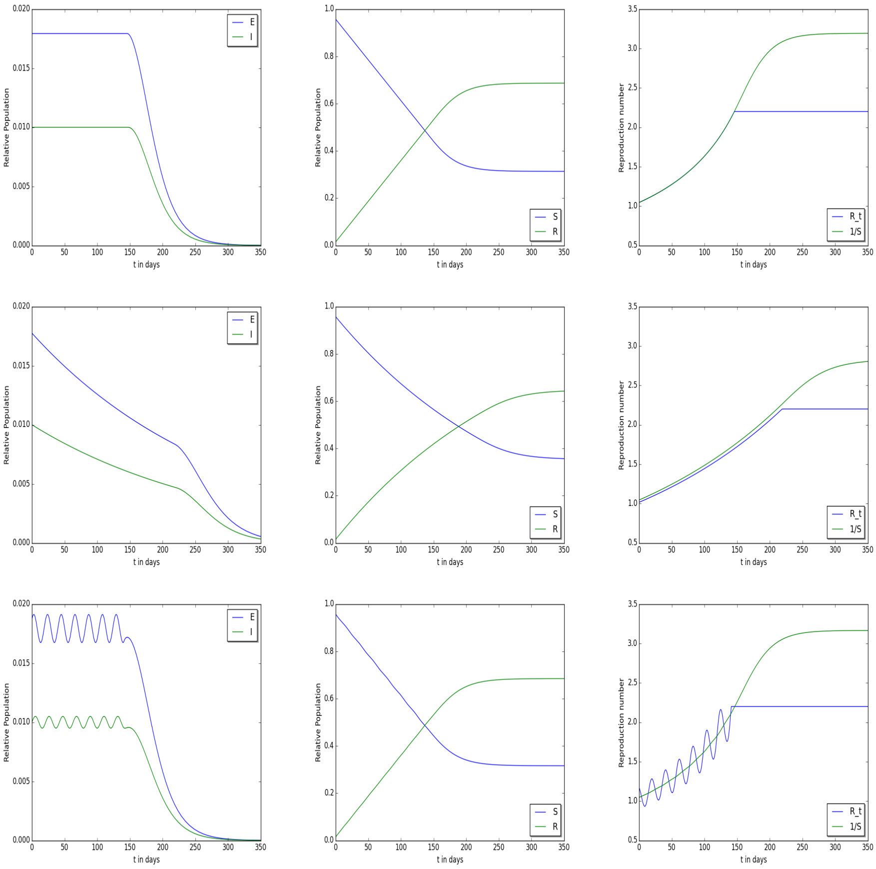

Figure 2: Some results for a constant (top), exponentially decreasing (middle) and periodic (bottom) function i, c.f. Section 4.

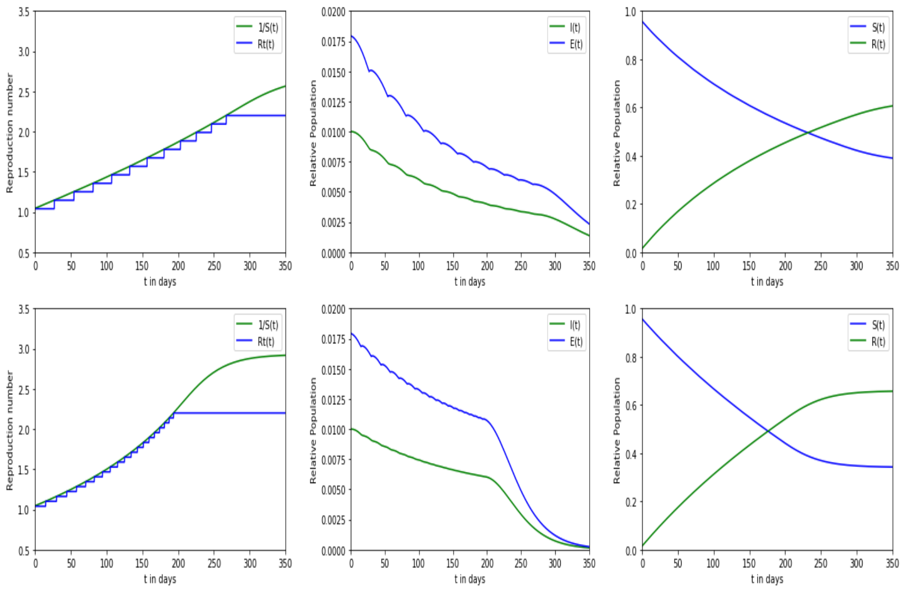

Figure 3: Some results for 12 and 20 constant and equidistant values of R_t for the controlled SEIR-ODE obtained with the code from the Appendix. The similarity to the results obtained in Figure 2 for the exponentially decreasing i is highly visible.

5 A Control Strategy for the ODE-Formulation

Since in practice $\mathcal{R}_t$ will not be a continuous function, in the following we assume that it is a piecewise constant function, where the constant values may depend on the social distancing policies. If these constant values are given, then a control strategy to increase $\mathcal{R}_t$ at the time-point at which $\frac{1}{S}$ is large enough can be easily be implemented considering the original SEIR-ODE (1)-(4). The results are presented in Figure 3 and the corresponding Python-Code can be found in the Appendix.

Of course, in practice the estimation of these constant values for $\mathcal{R}_t$ in dependence of social distancing policies and a good estimation of S will be crucial for the applicability of such a model.

6 Summary

In this article we outlined how a DAE-approach might be helpful for a better understanding of SEIR-ODEs and estimated an optimal choice of $\mathcal{R}_t$. This approach should be analogous for more sophisticated models with a realistic fitting of the parameters. Note that no rigorous bibliographical studies have been undertaken.

Acknowledgment

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References

[1] http://blog.ifac-control.org/control/coronavirus-policy-design-for-stable-population-recovery/

[2] http://gabgoh.github.io/COVID/index.html

[3] D. Estévez Schwarz and R. Lamour: Projected Explicit and Implicit Taylor Series Methods for DAEs. Preprint 2019-08, Fachbereich Mathematik, Humboldt-Universität zu Berlin.

Appendix

```
import matplotlib.pyplot as plt
import numpy as np
from scipy.integrate import solve_ivp


def SEIR_controlled(t,y):
    #Parameter
    Tinc=5.20 # Length of incubation period
    Tinf=2.9  # Duration patient is infectious

    S=y[0]
    E=y[1]
    I=y[2]
#    R=y[3] not used

    f=np.zeros(4)

    Rt=compute_Rt(S) # Compute R_t in dependence of S

    # SEIR-ODE
    f[0]  = -Rt/Tinf*I*S
    f[1]  = +Rt/Tinf*I*S-E/Tinc
    f[2]  = +E/Tinc-I/Tinf
    f[3]  = +I/Tinf

    return f

def compute_Rt(S):
    # compute maximal Rt (for given values Rn) with Rt leq 1/S

    R0=2.2  # value without social distancing
```

```
    Rt=1.04 # starting value, should be < 1/S0

    na=12 # number of adjustments
    Rn=np.linspace(Rt,R0,na)  # values for Rt
    # depending on social distancing, etc.
    # It is not necessary to choose Rn equidistant!

    for rn in Rn:
        if rn < 1/S:
            Rt=min(R0,rn)
    return Rt

if __name__=="__main__":


    ##############################################
    # Initialization
    ##############################################

    t_span=[0.0,350.0] # time interval in days

    I0=0.01

    Tinc=5.20 # Length of incubation period
    Tinf=2.9 # Duration patient is infectious
    E0=I0/Tinf*Tinc # then I'(t_0)=0

    R0=0.015
    S0=1.0-E0-I0-R0

    y0 = np.array( [S0,E0,I0,R0]) # initiall values


    ##############################################
    # Solve initial value problem
    ##############################################

    sol_ivp=solve_ivp(SEIR_controlled,t_span,y0,rtol=1.e-8,atol=1.e-8)


    ##############################################
    # Plot results
    ##############################################

    plt.figure(0)

    plt.plot(sol_ivp.t,sol_ivp.y[2,:], 'g', label='I(t)')
    plt.plot(sol_ivp.t,sol_ivp.y[1,:], 'b', label='E(t)')
    plt.axis([t_span[0],t_span[1], 0., 0.02])
    plt.legend(loc='best')
```

```python
plt.xlabel('t in days')
plt.ylabel('Relative Population')

plt.figure(1)

plt.plot(sol_ivp.t,sol_ivp.y[0,:], 'b', label='S(t)')
plt.plot(sol_ivp.t,sol_ivp.y[3,:], 'g', label='R(t)')
plt.axis([t_span[0],t_span[1], 0., 1.0])
plt.legend(loc='best')
plt.xlabel('t in days')
plt.ylabel('Relative Population')

plt.figure(2)

# Compute 1/S and R_t for plot
ln=len(sol_ivp.t)
invS=np.zeros(ln)
Rt=np.zeros(ln)
for k in range(ln):
    invS[k]=1./sol_ivp.y[0,k]
    Rt[k]=compute_Rt(sol_ivp.y[0,k])

plt.plot(sol_ivp.t,invS, 'g', label='1/S(t)')
plt.plot(sol_ivp.t,Rt, 'b', label='Rt(t)')
plt.axis([t_span[0],t_span[1], 0.5, 3.5])
plt.legend(loc='best')
plt.xlabel('t in days')
plt.ylabel('Reproduction number')

#plt.grid()
plt.show()
```