Section 5x. ODEs and COVID-19

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MACM 316: Numerical Analysis
Section 5x. ODEs and COVID-19

What do (ordinary) differential equations (ODEs) and COVID-19 have in common?

- Like many other physical and biological systems, the spread of an infectious disease can be described mathematically

  ... as functions of time

- Rates of change – rates of contact, infection, spread, recovery, etc. – can be described using time derivatives \( \Rightarrow \) leads naturally to differential equations

- Models of disease transmission are used to study, treat and manage epidemics:
  * by health agencies to minimize infections and optimize healthcare delivery
  * by drug companies to develop new drugs or treatment strategies
  * by news agencies to explain these issues to the public

... and we’ve all heard lots about the importance of “flattening the curve” by “social distancing”!

![Diagram showing the impact of protective measures on the number of cases](Adapted from CDC / The Economist)
Warning

• What I’ll describe is only a “toy model” for epidemics that has
  * many hidden assumptions
  * many approximations
  * several unknown parameters

• It can reproduce some (not all) realistic behaviours qualitatively

• BUT to make accurate predictions or reliable health-related decisions requires a real disease expert who is also intimately familiar with the mathematical models
  … and that’s definitely not me!!
Ordinary Differential Equations (ODEs)

- ODE’s are equations that involve:
  - a continuous function \( u(t) \) of a single variable \( t \), and
  - any of its derivatives \( \frac{du}{dt}, \frac{d^2u}{dt^2}, \ldots \)

- We will focus on first-order, ordinary differential equations having the form

\[
\frac{du}{dt} = f(t, u)
\]

  - first-order because only first derivatives are involved, AND
  - ordinary because \( u(t) \) depends on \( t \) only, so \( u' \) is an “ordinary” derivative.

**Aim:** To solve the initial value problem (IVP) consisting of an ODE and an initial condition:

\[
\frac{du}{dt} = f(t, u) \quad \text{for } 0 \leq t \leq t_{\text{max}}, \text{ subject to } u(0) = u_0
\]

**Examples:**

- \( \frac{du}{dt} = au \)
  - exponential growth/decay
- \( \frac{du}{dt} = au(1 - u) \)
  - logistic equation
- \( \frac{du}{dt} = \cos(t) + \frac{u^2}{1+u^2} \)
  - ... and anything else you can think of

(you have likely seen ODEs already in 152/155/158 or MATH 310 or ... )
Example 1: A Simple ODE IVP

Consider the first-order ODE initial value problem:

\[ u' = tu - \frac{t^3}{3} \quad \text{for} \quad 0 \leq t \leq \frac{[t_{\text{max}}]}{2.25} \quad \text{with} \quad u(0) = \frac{u_0}{0.5} \]

- This problem has exact solution \( u(t) = \frac{4 + 2t^2 - e^{t^2/2}}{6} \)
- Verify by substituting:

\[
\begin{align*}
\text{LHS} &= u' \\
&= 4t - te^{t^2/2} \\
&= \frac{4t - te^{t^2/2}}{6} \\
\text{RHS} &= t \left( \frac{4 + 2t^2 - e^{t^2/2}}{6} \right) - \frac{t^3}{3} \\
&= 4t - te^{t^2/2} \quad \text{with} \quad IC = u(0) = \frac{4 + 2(0)^2 - e^0}{6} = 0.5
\end{align*}
\]

**IVPs:** Think of \( t \) as time so that only \( t \geq 0 \) makes sense.
Euler’s Method

• Partition time $0 \leq t \leq t_{\text{max}}$ into $n$ intervals of equal length $h = \frac{t_{\text{max}}}{n}$ with
  
  $$t_j = jh \text{ for } j = 1, 2, \ldots, n - 1 \implies t_0 = 0 \text{ and } t_n = t_{\text{max}}$$

• $h$ is usually called the time step, even if $t$ is not time

• Evaluate the ODE $u' = f(t, u)$ at $t = t_0$, replacing $u'$ with a forward difference approximation:
  
  $$\frac{u(t_1) - u(t_0)}{h} \approx f(t_0, u(t_0)) \implies u(t_1) = u_0 + h f(t_0, u(t_0))$$

• Simplify notation: $u(t_j) \rightarrow u_j$ for $j = 0, 1, 2, \ldots, n$:

  $$u_1 = u_0 + h f(t_0, u_0)$$
  $$u_2 = u_1 + h f(t_1, u_1)$$
  $$\vdots$$
  
  $$u_{j+1} = u_j + h f(t_j, u_j) \quad \text{[ a step-by-step algorithm!]}$$

implies called the “Forward Euler Method” just or “Euler’s Method”
Example 1b: Apply Euler’s Method

Return to Example 1:

\[ u' = tu - \frac{t^3}{3} \]

with \( 0 \leq t \leq 2.25 \)

\[ u(0) = 0.5 \]

Take \( h = 0.25 \) and organize calculations in tabular form . . .

| j | \( t_j \) | \( u_j \) | \( f(t_j, u_j) \) | exact \( u(t_j) \) | abs. error \( |u_j - u(t_j)| \) |
|---|---|---|---|---|---|
| 0 | 0.00 | 0.500000 | 0.000000 | 0.500000 | — |
| 1 | 0.25 | 0.500000 | 0.119792 | 0.515543 | 0.015543 |
| 2 | 0.50 | 0.529948 | 0.223307 | 0.561142 | 0.031194 |
| 3 | 0.75 | 0.585775 | 0.298706 | 0.633369 | 0.047594 |
| 4 | 1.00 | 0.660451 | 0.327118 | 0.725213 | 0.064762 |
| 5 | 1.25 | 0.742231 | 0.276747 | 0.823467 | 0.081236 |
| 6 | 1.50 | 0.811417 | 0.092126 | 0.903297 | 0.091880 |
| 7 | 1.75 | 0.834449 | -0.326173 | 0.916841 | 0.082392 |
| 8 | 2.00 | 0.752906 | -1.160855 | 0.768491 | 0.203393 |
| 9 | 2.25 | 0.462692 | -2.755818 | 0.259299 | 0.203393 |

MATLAB: odeex1b.m on Canvas
MATLAB Code for Euler’s Method

This is a condensed version of the MATLAB code `odeex1b.m`:

```matlab
f = @(t,u) t.*u - t.^3/3; % RHS function for u'=f(t,u)

tmax= 2.25; % end time
nt = 9; % # steps
h = tmax / nt;% time-step
t = [0 : h : tmax];
u = zeros(1,nt+1);
u(1)= 0.5; % initial value u(0)

% Forward Euler time-stepping loop
for j = 1 : nt,
    u(j+1) = u(j) + h * f(t(j), u(j));
end

% Plot the computed solution
plot(t, u, ’ro’)
```
COVID-19 in the News

Plots like the ones below are ubiquitous in the news right now:

**DELAYING THE ONSET**
A simple mathematical model based on the characteristics of COVID-19 shows how reduced transmission through public-health measures (social distancing) can moderate and delay the onset of peak infection. However, this does not take into account the possibility that social distancing will loosen over time, which could generate a second peak, or the unknown effect of the changing seasons on virus transmission.

*Source: Globe & Mail, 16 March 2020 (https://tinyurl.com/vr4dy2g)*

*Adapted from CDC / The Economist*

*Source: The Late Show with Stephen Colbert, 17 March 2020*

Where do they come from?
Modelling Disease Transmission with ODEs

- A common mathematical model for disease transmission is the SEIR model.
- Population is divided into “compartments” (fractions of population) that vary with time:
  \[ S(t) = \text{Susceptible} \]
  \[ E(t) = \text{Exposed} \]
  \[ I(t) = \text{Infectious} \]
  \[ R(t) = \text{Recovered} \]
  
  with \( S + E + I + R = 1 \) \( \rightarrow \) total population remains constant!

- The rates of change of each fraction are determined by rate / transfer laws:
  
  * Interactions between people in two compartments \((x, y)\) occur with probability proportional to \(x \times y\)
  * Suppose interactions cause a transfer from \(x \rightarrow y\). Then the rate of transfer is \( \pm (\text{const}) \times x \times y\)
    \[ \Rightarrow \quad \frac{dx}{dt} = -\alpha xy \quad \text{and} \quad \frac{dy}{dt} = +\alpha xy \quad \text{[“conservation of people”]} \]
  
  * Simpler transfers \(x \rightarrow y\) with no interactions obey a simpler rate law:
    \[ \Rightarrow \quad \frac{dx}{dt} = -\alpha x \quad \text{and} \quad \frac{dy}{dt} = +\alpha x \]
SEIR Transmission Steps

**Step 1:** Susceptibles become exposed \((S \rightarrow E)\) due to \(S/I\) interactions at a contact rate \(\beta\):

\[
\frac{dS}{dt} = -\beta SI
\]

**Step 2:** Susceptibles become exposed \((S \rightarrow E)\) at same rate \(\beta\) and exposeds become infectious \((E \rightarrow I)\) at an infection rate \(\alpha\):

\[
\frac{dE}{dt} = +\beta SI - \alpha E \quad \alpha = \frac{1}{(\text{average incubation period})}
\]

**Step 3:** Exposeds become infectious \((E \rightarrow I)\) and infectious people also recover \((I \rightarrow R)\) at a recovery rate \(\gamma\):

\[
\frac{dI}{dt} = +\alpha E - \gamma I \quad \gamma = \frac{1}{(\text{average infectious period})}
\]

**Step 4:** Infectious become recovered \((I \rightarrow R)\):

\[
\frac{dR}{dt} = +\gamma I
\]

- So far ... no-one dies from the virus
- That’s unrealistic BUT the death rate is small
Vector Form

• Define the solution as a vector function

\[ \vec{u}(t) = \begin{bmatrix} u_1(t) \\ u_2(t) \\ u_3(t) \\ u_4(t) \end{bmatrix} = \begin{bmatrix} S(t) \\ E(t) \\ I(t) \\ R(t) \end{bmatrix} \]

• Rewrite the system of four ODEs as in vector form

\[ \frac{d\vec{u}}{dt} = \vec{f}(\vec{u}) \]

\[ \begin{bmatrix} \frac{dS}{dt} \\ \frac{dE}{dt} \\ \frac{dI}{dt} \\ \frac{dR}{dt} \end{bmatrix} = \begin{bmatrix} -\beta SI \\ \beta SI - \alpha E \\ \alpha E - \gamma I \\ \gamma I \end{bmatrix} \quad \Rightarrow \quad \frac{d\vec{u}}{dt} = \begin{bmatrix} -\beta u_1 u_3 \\ \beta u_1 u_3 - \alpha u_2 \\ \alpha u_2 - \gamma u_3 \\ \gamma u_3 \end{bmatrix} = \vec{f}(\vec{u}) \]

• Euler’s method is applied component-wise to systems of ODEs
Model Parameters for COVID-19

We start with some very rough estimates of the parameters:

- Rate of incubation: \( \alpha = 0.2 \)  
  [ incubation period of 5 days ]

- Average S/I contact rate: \( \beta = 1.75 \)

- Rate of recovery: \( \gamma = 0.5 \)  
  [ infectious period is 2 days ]

- Reproduction number: \( R_0 = \frac{\beta}{\gamma} = 3.5 \)

- Total population: \( N_0 = 10,000 \)

- Initial values: \( \vec{u}(0) = [1 - 1/N_0, 0, 1/N_0, 0] \)  
  [ start with one infectious person ]

[ Based on literature cited in Christian Hubbs’ blog post ]
alpha = 0.2; % incubation period (5 days)
beta = 1.75; % average contact rate
gamma = 0.5; % 1/gamma is mean infectious period (2 days)
R0 = beta/gamma; % reproduction number

% Normalized population with S+E+I+R = 1.
N0 = 10000; % initial population, one person infectious
u0 = [1-1/N0, 0, 1/N0, 0]; % initial values with sum(u0)=1

% RHS function for the SEIR ODE with u=[S,E,I,R]
f = @(u) [-beta*u(1)*u(3), beta*u(1)*u(3)-alpha*u(2), ...
alpha*u(2)-gamma*u(3), gamma*u(3)];

dt = 0.1;
t = [0 : dt : 100]';
nt = length(t)-1;
u = zeros(nt+1, 4);
u(1,:) = u0; % initialize SEIR values

% Euler time-stepping loop
for k = 1 : nt,
    u(k+1,:) = u(k,:) + dt * f(u(k,:));
end
Play Around!

Original parameters
(5-day incubation & 2-day infectious period)

Decrease $\gamma : 0.5 \rightarrow 0.05$
(20-day infectious period)

Decrease $\alpha : 0.2 \rightarrow 0.05$
(20-day incubation period)

BOTH: $\alpha = \gamma = 0.05$
Exponential Growth of Infections . . . Initially!

- Early stages of an epidemic exhibit exponential growth
- Infections must eventually slow down (population is finite)
- BUT predicting / identifying the turn-around or inflection point is difficult

**Key Question:** Where on the infection curve are we sitting NOW?

[Image of Active Cases in the United States chart]

https://www.worldometers.info/coronavirus

Excellent video by minutephysics: “How to tell if we’re beating COVID-19”
https://youtu.be/54XLXg4fYsc
When is the Infection Slowing Down?

It can be difficult to identify when the exponential growth is starting to turn around.
Reproduction Number \( R_0 \)

A common measure of how infectious a disease is:

- \( R_0 = \frac{\beta}{\gamma} \) is the expected number of cases resulting from one infectious case in a population where everyone is susceptible to infection.

- Basic theoretical results:
  * If \( R_0 > 1 \), the infection can spread in a population.
  * If \( R_0 < 1 \), the infection dies out naturally.
  * The larger \( R_0 \) is, the harder it is to control an epidemic.

- \( R_0 \) can’t be determined from data – it’s estimated from SEIR model simulations.

- Compare the estimate of \( R_0 \approx 3.5 \) for COVID-19 to past epidemics:

  ![Graph comparing R0 values for different diseases]

  More Contagious

  - Hepatitis C (2)
  - Ebola (2)
  - HIV (4)
  - SARS (4)
  - Mumps (10)
  - Measles (18)
Importance of Social Distancing

- Social distancing is being promoted as an effective measure to control the COVID-19 virus by reducing the S/I contact rate $\beta$ [same effect as reducing $R_0 = \beta/\gamma$]
- Mimic social distancing by replacing $\beta \rightarrow \rho \beta \implies$ simulate with $\rho = 1.0, 0.8, 0.6$

**Effect of social distancing ($\rho$)**

![Graph showing the effect of social distancing on the population fraction over time. The graph compares the population fraction of exposed and infectious individuals with different values of $\rho$.](image)
Reality is Much More Complicated

Many other effects can be added to such models that increase complexity:

- deaths and births $\implies S + E + I + R \neq 1$
- maternally inherited immunity at birth $\implies$ MSEIR model
- age-structured population $\implies$ different contact / infection / recovery / death rates
- time-varying transmission $\implies$ parameters depend on $t$
- effects of hospitalization / treatment / vaccination
- differences in geography and national response $\implies$ add spatial dependence
- political response to (and politicization of) results of disease models!!

“Coronavirus modelers factor in new public health risk: Accusations their work is a hoax”
Washington Post, March 27, 2020
https://tinyurl.com/sd439w5
References


- Wikipedia, “Compartmental models in epidemiology”.

