Lecture 24: **If an equation cannot be solved...**

Learning objectives

✓ Understand how to find an approximate solution when an equation cannot be solved analytically

✓ Understand how to apply Newton's method

Scientific examples

✓ Depo-Provera for contraception

Maths skills

✓ Understand Newton's method and how to use it

9.3 Derivatives and Newton's method

Case Study 19: **Contraceptive calculations**

Photo 9.3: Various types of contraceptive including: oral contraceptive, condoms, injected contraceptives and traditional herbal methods. (Source: PA.)

- Each of the many different methods of contraception has advantages and disadvantages.

- Table 9.2 compares the effectiveness of various methods of contraception, based on data given in [10].

Method	Typical use	Ideal use	1-year
Chance	85	85	
Spermicides	26	6	40
Periodic Abstinence	25	1 – 9	63
Cap			
Parous Women	40	26	42
Nulliparous Women	20	9	56
Sponge			
Parous Women	40	20	42
Nulliparous Women	20	9	56
Diaphragm	20	6	56
Withdrawal	19	4	
Condom	14	3	61
Oral pill	5	0.1	71
IUD	0.1 – 2.0	0.1 – 1.5	80
Depo-Provera IM 150 mg	0.3	0.3	70
Female Sterilisation	0.5	0.5	100
Male Sterilisation	0.15	0.10	100

Table 9.2: The expected percentage of women who will experience an unintended pregnancy when using various methods of contraception for a year, through either typical use or ideal (very careful) use. Also shown is the average percentage of women continuing to use that method of contraception after one year.

- Depo-subQ Provera 104 is a long-term female contraceptive administered as an injection every 12 – 13 weeks.

- The active ingredient in a standard 0.65 mL dose is 104 mg of the artificial female hormone medroxyprogesterone acetate (MPA), which is similar to progesterone.

- It is 99.7% effective, which is very high when compared to many other forms of contraception.

- Commonly quoted benefits are convenience and reliability.

- Studies have identified some side effects, including breakthrough bleeding, reduced libido, weight gain and potentially, reduced bone density.

Example 9.3.1

Table 9.3 shows some pharmacokinetic parameters of MPA after a single subcutaneous injection of Depo-SubQ Provera 104 in healthy women. The data are based on results in [10], with a sample size of $n = 42$ women.

	C_{max} (ng/mL)	t_{max} (day)	C_{91} (ng/mL)	AUC_{0-91} (ng day/mL)	$AUC_{0-\infty}$ (ng day/mL)	$t_{1/2}$ (day)
Mean	1.56	8.8	0.402	66.98	92.84	43
Min	0.53	2.0	0.133	20.63	31.36	16
Max	3.08	80.0	0.733	139.79	162.29	114

Table 9.3: Pharmacokinetic parameters of MPA.

lectures next week

In Table 9.3:

- C_{max} = peak blood concentration;
- t_{max} = the time at which C_{max} occurs;
- C_{91} = blood concentration at 91 days; = 13 weeks
- AUC_{0-91} = the area under the concentration-time curve over 91 days;
- $AUC_{0-\infty}$ = the area under the concentration-time curve over an indefinite time period; and
- $t_{1/2}$ = half-life removal of MPA from the body.

Question 9.3.2

The blood concentration of an injected long-lasting female contraceptive (medroxyprogesterone acetate or MPA) in ng/mL can be modelled by the function $C(t) = 1.4t^{0.15}e^{-0.02t}$. The graph of $C(t)$ is shown in Figure 9.4.

surge

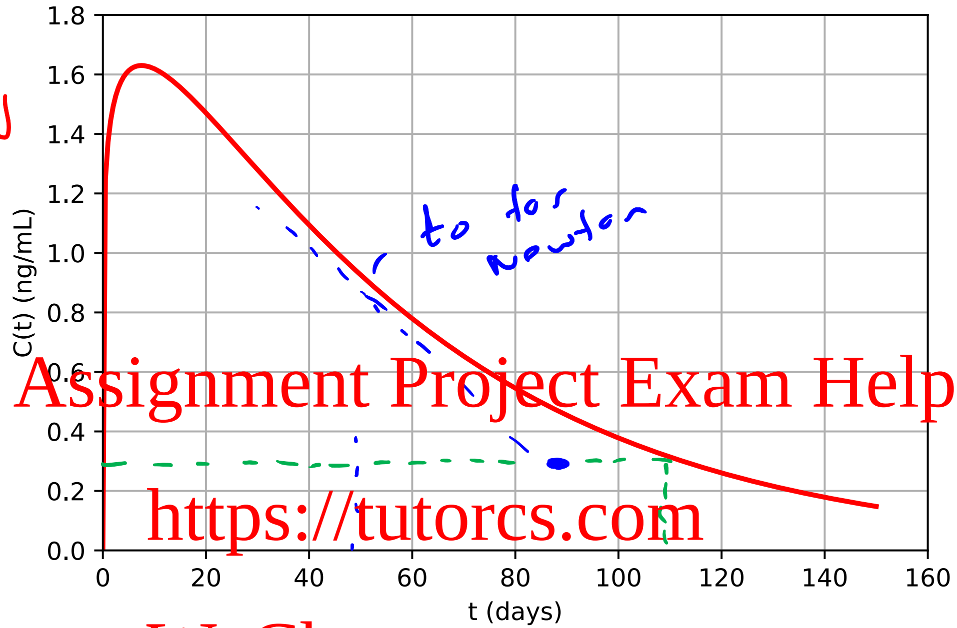


Figure 9.4: Modelled blood concentration after an injection of MPA.

(a) The minimum blood concentration for reliable contraception is 0.3 ng/mL. Estimate the time at which reliable contraception ceases.

Drops below 0.3 ng/mL after about 110 days

(b) Write an equation that should be solved to accurately find this time.

$$C(t) = 0.3 \Rightarrow 1.4t^{0.15}e^{-0.02t} = 0.3$$

(c) Do you think you could solve the equation in Part (b)?

Analytically not solveable!

- Some equations are difficult or impossible to solve **exactly**. An alternative is to find an **approximate** solution, using *solution-finding* algorithms, which involve repeatedly applying similar mathematical steps or *iterations.*

- Usually, a *numerical error* is associated with the approximate solutions. These errors can often be reduced by performing more iterations.

- *Newton's method* is an iterative solution-finding algorithm which uses an *initial estimate* of a solution and a derivative to find a solution. Newton's method does not always *converge* to a solution, but will usually converge if the initial estimate is 'good enough'.

- Note that Newton's method only solves equations of the form $\boxed{f(x) = 0.}$ Before applying Newton's method, the equation may need rearranging. For example, to use Newton's method to solve the equation in Part (b) of Question 9.3.2, we instead solve $\underbrace{C(t) - 0.3}_{f(t)} = 0$.

$C(t) = 0.3$

$f(t) = C(t) - 0.3$

$f(t) = 0$

Newton's method - informal description

To solve $f(x) = 0$:

graph → approximate value

1. Choose an initial estimate of the solution. – experience

2. Calculate a new estimate using the old estimate and the derivative. (The new estimate is hopefully better than the old.)

fail

3. Stop if the new estimate is "sufficiently accurate" or if $\boxed{\text{too many steps}}$ have been taken. Otherwise, return to Step 2.

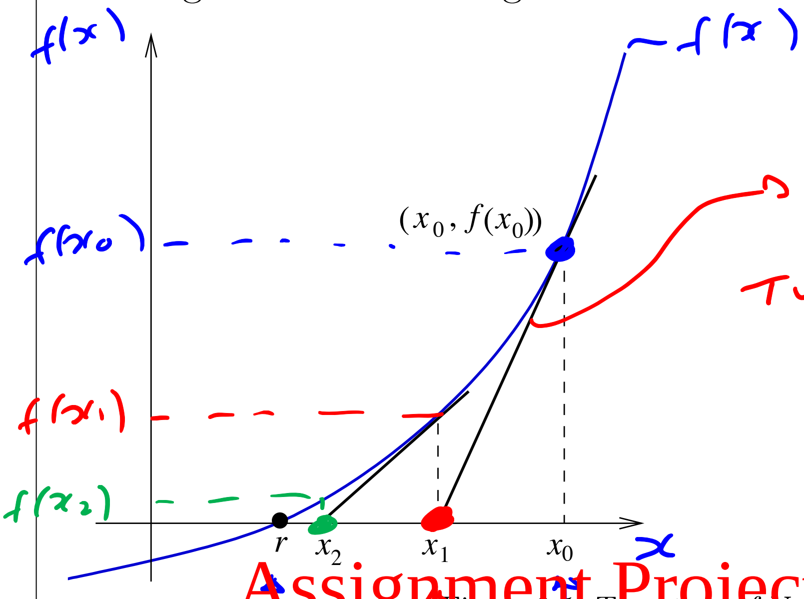
needs defining

- Newton's method is based on equations of straight lines!

- Let the initial estimate of an unknown solution of $\boxed{f(x)}$ be $\boxed{x_0}$. Newton's method calculates the next estimate $\boxed{x_1}$ by extending a line from the point $\boxed{(x_0, f(x_0))}$ to the x-axis, with the slope of the line equal to the value of the derivative f' at the point x_0; see Figure 9.5.

Question 9.3.3

Annotate the following figure to describe how Newton's method repeatedly uses a guess and the tangent line to find the next guess.



Know $f(x)$, $f'(x)$

$f'(x) = \text{slope} = m$

straight line

$\text{slope} = \frac{\text{rise}}{\text{run}}$

Two points $(x_0, f(x_0))$

$(x_1, 0)$

$\text{slope} = f'(x_0) = \frac{f(x_0) - 0}{x_0 - x_1}$

$x_0 - x_1 = \frac{f(x_0)}{f'(x_0)}$

Figure 9.5: Two steps of Newton's method.

$x_1 = x_0 - \frac{f(x_0)}{f'(x_0)}$

all known

repeat!

Newton's method - formal description

To solve $f(x) = 0$:

1. Let x_0 be an initial estimate of a solution of f that is 'sufficiently close' to an actual solution of f. At the ith iteration ($i = 0, 1, 2, \ldots$), x_i is the current approximation of the actual solution.

2. Calculate the next estimate: $$\boxed{x_{i+1} = x_i - \frac{f(x_i)}{f'(x_i)}}$$

3. (a) If the value of x_{i+1} is "sufficiently accurate" then stop; x_{i+1} is the estimated solution.

(b) If x_{i+1} is not "sufficiently accurate" after a certain number of steps then stop, because the method is probably not converging to a solution. Choose a 'better' value for x_0 and start again.

(c) Otherwise, return to Step 2.

$\cancel{x - \sqrt{12} = 0}$

***Example** 9.3.4*

Use Newton's method to estimate $\boxed{x = \sqrt{12}}$.

Newton's method is used to solve equations of the form $\boxed{f(x) = 0}$. We want to solve $x = \sqrt{12}$, which does not have the right form. However, we know that $x = \sqrt{12}$ will be a solution to $\boxed{x^2 - 12 = 0}$, and this equation has the form for Newton's method. Hence, let $\boxed{f(x) = x^2 - 12}$; we aim to solve $f(x) = 0$.

To apply Newton's method, we first need to find the derivative and then choose an initial estimate of the solution:

- Because $\boxed{f(x) = x^2 - 12}$, we have $\boxed{f'(x) = 2x}$.
- We know that $\sqrt{12}$ is between 3 and 4 so we will use $\boxed{x_0 = 3}$ as the initial estimate of the solution. (We could choose other estimates but $x_0 = 3$ is likely to be "close" to the solution.)

Now we have everything we need to use Newton's method. Recall that the equation for finding the next estimate of the solution is:

$$x_{i+1} = x_i - \frac{f(x_i)}{f'(x_i)}.$$

RHS is known

Performing three steps of Newton's method gives the results shown in Table 9.4, with the last column showing the sequence of approximations to the solution.

$x_0 = 3$, $f(x_0) = f(3) = (3)^2 - 12 = -3$

$f'(x_0) = f'(3) = 2(3) = 6$

i	x_i	$f(x_i) = x_i^2 - 12$	$f'(x_i) = 2x_i$	x_{i+1}
0	3	−3	6	3.5
1	3.5	0.25	7	3.4642857
2	3.4642857	0.001275	6.92857	3.4641016

Table 9.4: Using three iterations of Newton's method to find $\sqrt{12}$.

$x_1 = x_0 - \frac{f(x_0)}{f'(x_0)}$

$= 3 - \frac{(-3)}{6}$

$= 3.5$

After three steps, the estimate of $\sqrt{12}$ is $x_3 = 3.4641016$ which is actually accurate to seven decimal places.

- We will now return to finding the time at which reliable contraception ceases after an injection of MPA. To do this, we will use derivatives and Newton's method to solve the equation thus determine the timing of a follow-up injection.

- Reliable contraception ceases when $C(t) = 0.3$ ng/mL, so $\overbrace{C(t) - 0.3}^{f(t)} = 0$ and hence the function $f(t)$ for Newton's method is:

$$f(t) = \underbrace{1.4t^{0.15}e^{-0.02t}}_{c(t)} - \underbrace{0.3}_{\times}.$$

$f'(t) = c'(t)$

- The derivative is:

$$f'(t) = 1.4e^{-0.02t}\left(0.15t^{-0.85} - 0.02t^{0.15}\right).$$

- We can use $t_0 = 50$ days as the initial estimate for the solution. (Remember that you usually have a choice of many different initial values.)

Question 9.3.5

Use one step of Newton's method to find a "better" approximate solution to $f(t) = 0$ for this example.

we are given ..., find t_1

$$t_1 = t_0 - \frac{f(t_0)}{f'(t_0)}$$

$$= 50 - \frac{1.4(50)^{0.15}e^{-0.02(50)} - 0.3}{1.4e^{-0.02(50)}\left(0.15(50)^{-0.85} - 0.02(50)^{0.15}\right)}$$

$$= 50 + 39.8$$

$$= \underline{\underline{89.8 \text{ days}}}$$

A Python program can be written to perform further steps.

Program specifications: Write a Python program to apply Newton's method to find the follow-up time for a contraceptive injection.

Program 9.1: Using Newton's method for contraception

```python
# Use Newton's method to find the follow-up time for a
# contraceptive injection.
from pylab import *

# Define the function and its derivative.
def func(t):
    return 1.4 * pow(t,0.15) * exp(-0.02*t) - 0.3

def func_dash(t):
    val1 = 1.4 * exp(-0.02*t)
    val2 = 0.15 * pow(t,-0.85) - 0.02*pow(t,0.15)
    return(val1 * val2)

# Input initial estimate.
val = float(input("What is the initial estimate? "))

# Loop through steps of Newton's method.
i = 0
while abs (func(val)) > 0.0001:
    val = val - func(val) / func_dash(val)
    i = i + 1
    print("Step ",i,":",round(val,3))

# Ouput
print("Estimated time is:",round(val,3),"days")
```

f(t)

f'(t)

initial guess input

test "sufficiently close"

Newton's method

output

The program output is:

```
What is the initial estimate? 50
Step  1 : 89.769
Step  2 : 108.467
Step  3 : 112.302
Step  4 : 112.44
Estimated time is: 112.44 days
```

As seen, it gave: $t_4 \approx 112.440$ days after four steps. Thus, the blood concentration of MPA decreased to 0.3 ng/mL at around 112 days, or about 16 weeks (the manufacturer recommends 12-13 weeks with some safety margin).

End of Case Study 19: Contraceptive calculations.