AUC area under curve

Lecture 27: **Exposure and trapezoids**

Learning objectives

✓ Calculate and interpret the meaning of the area under a curve

Scientific examples

✓ Exposure to nicotine

✓ Exposure to glucose

Maths skills

✓ Estimate the area under a curve using rectangles

✓ Estimate the area under a curve using the trapezoid rule

- When a function is known, it may be possible to calculate the area under the curve using definite integrals. A brief reminder of this is included in Section C.5 of Appendix C.

- More often, AUCs are used in practical applications in which the only available information is a collection of measured data values, and the function $f(x)$ is **not** known. In such cases, AUCs are estimated approximately, by summing the areas of geometric shapes of "narrow" width, such as rectangles (called *Riemann sums*), or *trapezoids* (called the *trapezoid rule*).

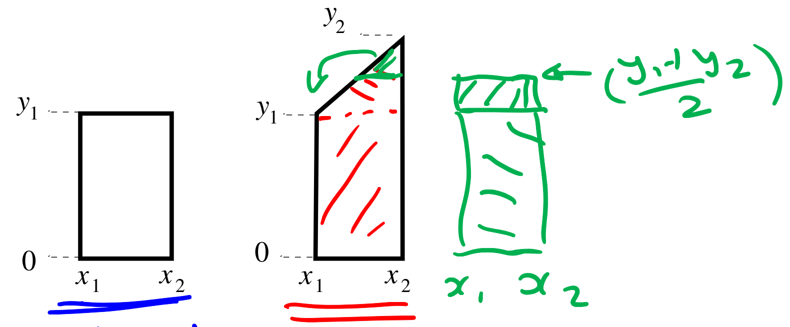
Question 10.1.4

Give some advantages and disadvantages of each way of finding AUCs.

	Integration	Summing geometric shapes
Pros	Exact Accurate	Can always be done (data points and/or function)
Cons	Need to know or fit a function	Not as accurate - approximation

Question 10.1.5

(a) Derive expressions for the areas of the rectangle and the trapezoid.



Rectangle:

area = base × height

$= (x_2 - x_1) \times (y_1 - 0)$

$= (x_2 - x_1)\, y_1$

Trapezoid

area = area rectangle + area triangle

$= (x_2 - x_1)\, y_1 + \frac{1}{2}(x_2 - x_1)(y_2 - y_1)$

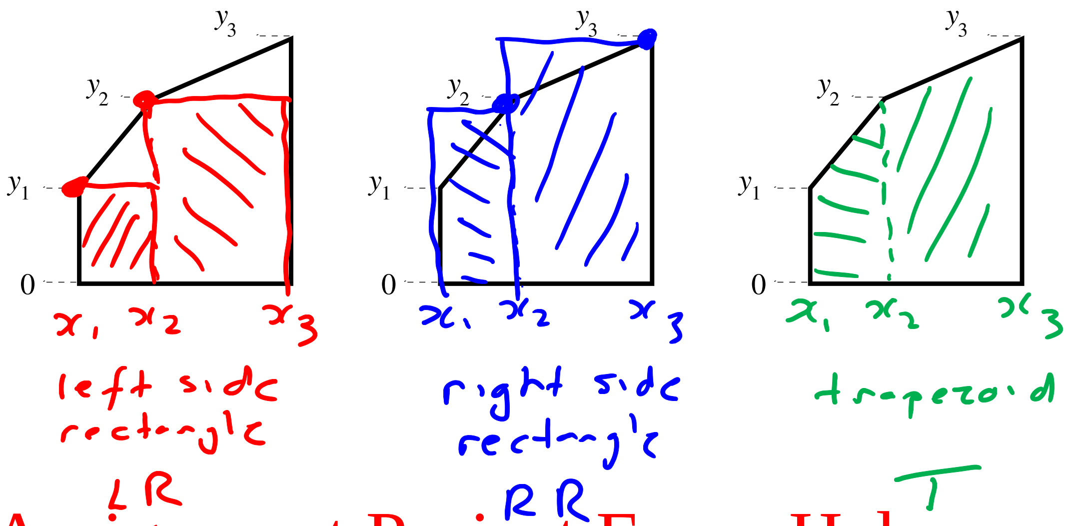
$= (x_2 - x_1)\left[y_1 + \frac{1}{2}(y_2 - y_1)\right]$

$= (x_2 - x_1)\left[y_1 + \frac{1}{2} y_2 - \frac{1}{2} y_1\right]$

$= (x_2 - x_1)\left(\frac{y_1 + y_2}{2}\right)$

***Question** 10.1.5 (continued)*

(b) Show how to find the approximate area of the following shape in three ways, using rectangles in two different ways, and using trapezoids.



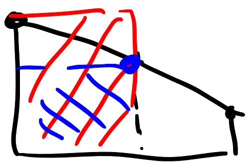
(c) Comment on the three approaches you used in Part (b). Which is likely to be most accurate? How do the two methods using rectangles relate to the method using trapezoids?

Trapezoid is most accurate

LR < T < RR

For a decreasing data points

LR > T > RR



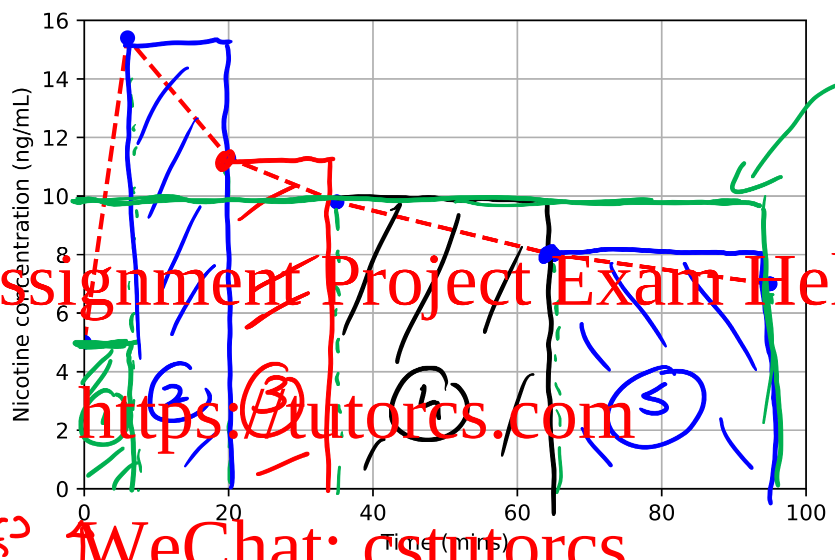
Question 10.1.6

Let $N(t)$ be an unknown function representing the blood nicotine concentration of a person after smoking a cigarette. Figure 10.3 shows some concentrations, measured experimentally (see [3]). Data points are joined by straight lines.

1

t (min.)	0	6	20	35	65	95
Value (ng/mL)	5	15.4	11.3	9.8	8	7

base x height



smoking ends

Figure 10.3: Measured blood nicotine concentrations after smoking.

The following calculations use areas of rectangles to estimate partially the AUC of the nicotine concentration curve. Link the calculations to rectangles on the graph and then complete the calculation for the remaining points.

base height

1) $(6-0) \times 5 = 30$ LR

2) $(20-6) \times 15.4 = 215.6$ LR

3) $(35-20) \times 11.3 = 169.5$ LR

4) $(65-35) \times 9.8 = 294$ LR

5) $(95-65) \times 8 = 240$ LR

AUC $= 949.1 \ \frac{\text{ng}}{\text{mL}}$ mins

Sense check?
one rectangle
(average height)
$10 \ \frac{\text{ng}}{\text{mL}} \times 95$ min
$\approx 950 \ \frac{\text{ng}}{\text{mL}}$ min

(over?)

Question 10.1.7

Repeat Question 10.1.6 but instead use the trapezoid rule.

t (min.)	0	6	20	35	65	95
Value (ng/mL)	5	15.4	11.3	9.8	8	7

AUC $= (x_2 - x_1)\left(\frac{y_1+y_2}{2}\right)$

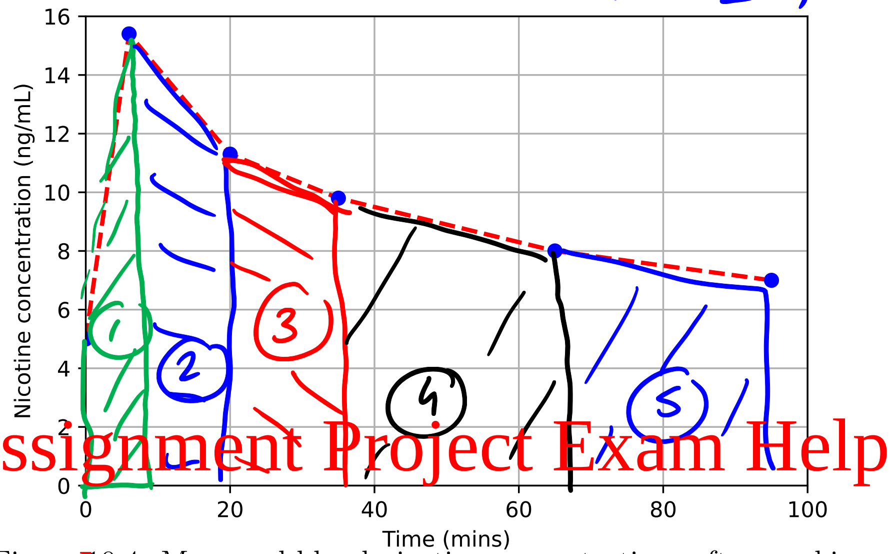


Figure 10.4: Measured blood nicotine concentrations after smoking.

1. $(6-0) \times (5+15.4)/2 = 61.2$
2. $(20-6) \times (15.4+11.3)/2 = 186.9$
3. $(35-20) \times (11.3+9.8)/2 = 158.25$
4. $(65-35) \times (9.8+8)/2 = 267.0$
5. $(95-65) \times (8+7)/2 = 225.0$

AUC $= 898.35 \ \frac{\text{ng}}{\text{mL}} \text{min}$

We can perform the previous calculations more efficiently using a program.

Program specifications: Write a Python program that estimates the AUC for $N(t)$ using rectangles or the trapezoid rule. The program must output the total AUC and draw a graph showing the shapes used in the sums.

Program 10.2: AUC for nicotine

```
# Use rectangles or trapezoids to estimate AUC for nicotine.
from pylab import *

# Initialise variables
shape = float(input("Type 1 for rectangles, 2 for trapezoids: "))
time = array([0, 6, 20, 35, 65, 95])
concentration = array([5, 15.4, 11.3, 9.8, 8, 7])
area = 0

# Sum the areas of each shape
i = 1
while i < size(time):
    width = time[i] - time[i-1]
    if shape == 1:
        height = concentration[i-1]
        shape_t = array([time[i-1], time[i-1], time[i], time[i]])
        shape_c = array([0, height, height, 0])
    else:
        height = (concentration[i-1] + concentration[i])/2
        shape_t = array([time[i-1], time[i-1], time[i], time[i]])
        shape_c = array([0, concentration[i-1], concentration[i], 0])
    area = area + height * width
# Plot each shape
    plot(shape_t, shape_c, "k-",linewidth=2)
    i = i + 1

# Finish plot and give the output.
print("The estimated AUC is",area,"ng min / mL")
plot(time, concentration, "bo", markersize=8)
xlim(0,100)
ylim(0,16)
xlabel("Time (mins)")
ylabel("Nicotine concentration (ng/mL)")
if type == 1:
    title("Blood concentration of nicotine (rectangles)")
else:
    title("Blood concentration of nicotine (trapezoids)")
show()
```

input + data

right rectangle

left rectangle

calc.

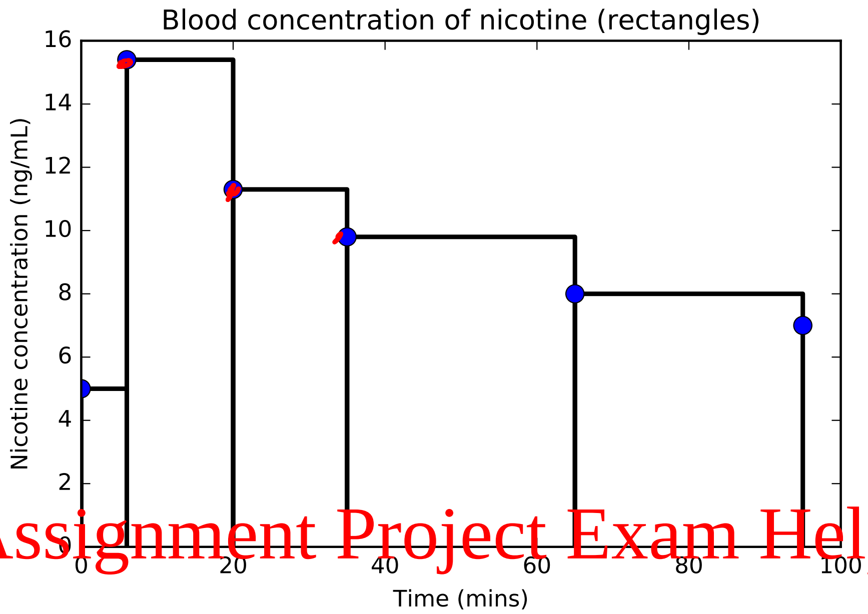
trapezoid

output

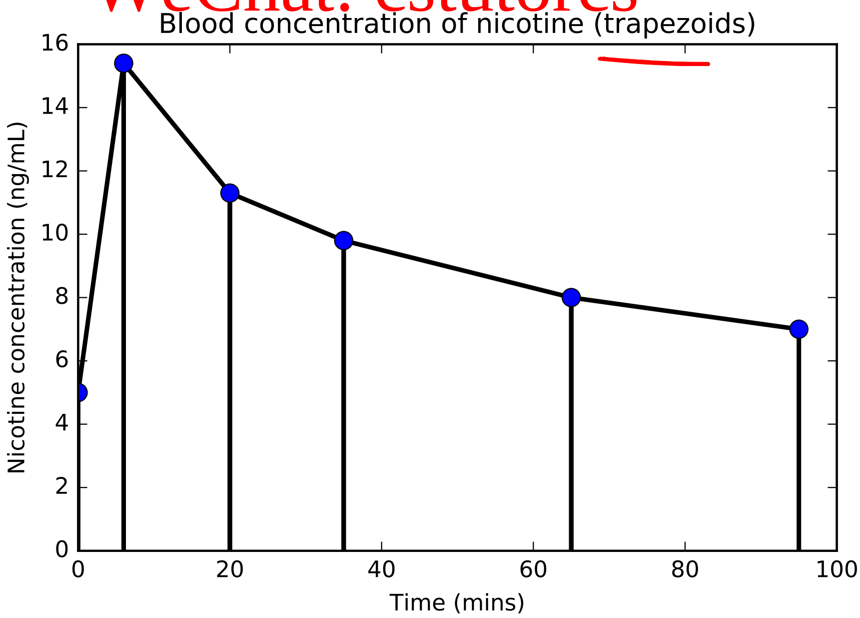
Here is the output from running the above program twice:

```
Type 1 for rectangles, 2 for trapezoids: 1
The estimated AUC is 949.1 ng min / mL
```

left




```
Type 1 for rectangles, 2 for trapezoids: 2
The estimated AUC is 898.35 ng min / mL
```

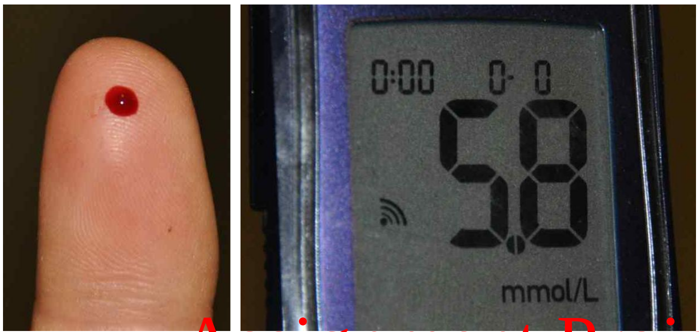



10.2 All in the blood

Case Study 22: **Sweet P's**

- The hormone *insulin* regulates conversion of glucose into usable energy in the body. *Diabetes mellitus* is a group of chronic diseases in which insufficient insulin is produced, or insensitivity to insulin develops. This leads to high levels of blood glucose.
- There are three main types of diabetes: *type 1* (insulin-dependent diabetes, typically present at birth, representing about 10–15% of all cases), *type 2* (non-insulin-dependent diabetes, which accounts for 85–90% of all cases) and *gestational diabetes* (developed in ~~3–8~~% of pregnancies). 15–20%
- Typical signs of diabetes include:
  - *polyuria* (excessive urination, often with a sweet taste)
  - *polydipsia* (excessive thirst)
  - *polyphagia* (excessive hunger).
- Once type 1 or type 2 diabetes becomes established, it is usually permanent.
- Diabetes, particularly type 2, is becoming increasingly common in societies with a "western lifestyle". Around 1.7 million Australians have diabetes, although only about half of them are aware of it.
- The Framingham heart study has shown that diabetes significantly reduces life expectancy (by 7.5 years for men aged over 50, and 8.2 years for women).
- Untreated diabetes can cause blindness, kidney failure and cardiovascular disease including blockages in small arteries. Some patients require amputations after blocked peripheral circulation causes the death of soft tissue.

- An *Oral Glucose Tolerance Test* (OGTT) is a common test for diabetes.
- Prior to taking the test, the patient fasts for around 12 hours. During the test, the patient is administered a measured oral dose of glucose, with blood samples taken immediately prior to ingestion of the glucose and at various intervals for 2 hours afterwards.
- The graph in Figure 10.5 compares the measured blood glucose levels for a non-diabetic person with those from a hypothetical diabetic person.



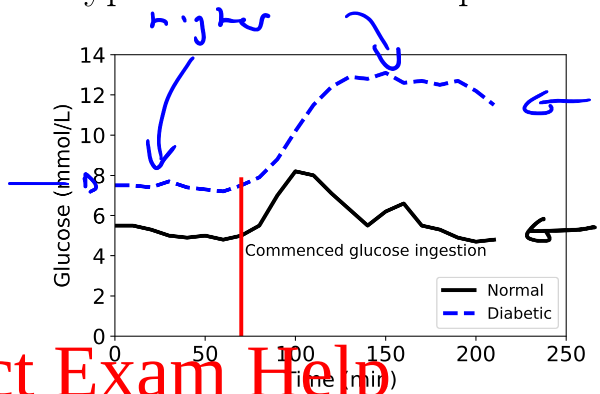


Photo 10.2: Left: bloody finger. Right: measured blood glucose concentration. (Source: PA.)

Figure 10.5: Normal blood glucose levels and levels indicative of diabetes.

- Table 10.1 shows the World Health Organisation guidelines for blood glucose levels indicating various stages of health or disease.

	Blood glucose level (mmol/L)			
time (hr)	Normal	IFG	IGT	DM
$t = 0$	< 6.1	$\geq 6.1, < 7.0$	< 7.0	≥ 7.0
$t = 2$	< 7.8	< 7.8	≥ 7.8	≥ 11.1

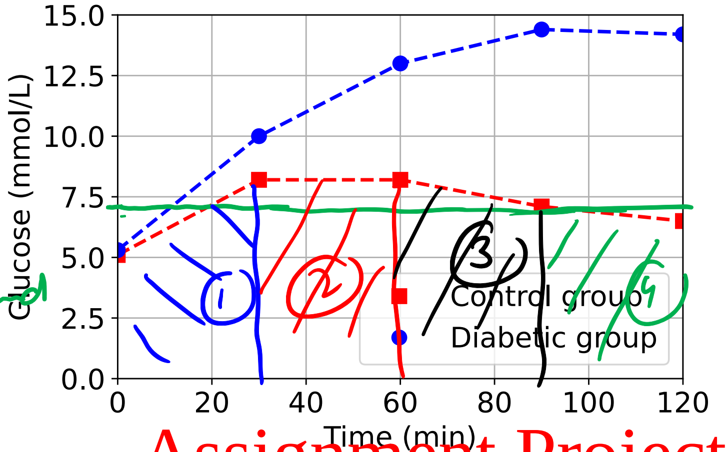
Table 10.1: World Health Organisation guidelines for blood glucose levels as indicators of: Impaired Fasting Glycaemia (IFG); Impaired Glucose Tolerance (IGT or *pre-diabetes*); and Diabetes Mellitus (DM).

- It is possible that an individual blood glucose measurement might be within the normal range at some instant in time, but outside that range over a longer time period. It is often very useful to analyse AUCs as well.

Question 10.2.1

Figure 10.6 shows measured blood glucose levels for a diabetic and control groups, adapted from [24]. Data points are interpolated by straight lines.

background



time (mins)	diabetic (mmol/L)	control (mmol/L)
0	5.3	5.1
30	10	8.2
60	13	8.2
90	14.4	7.1
120	14.2	6.5

Figure 10.6: Mean blood glucose levels for diabetic and non-diabetic (control) groups.

(a) Roughly estimate the AUC for the control group.

AUC = (120) × (7) ≈ 840 $\frac{mmol}{L}$ min

(b) Use the trapezoid rule to calculate the AUC for the control group.

(1) $(30-0) \times \left(\frac{5.1+8.2}{2}\right) = 199.5$

(2) $(60-30) \times \left(\frac{8.2+8.2}{2}\right) = 246$ (rectangle)

(3) $(90-60) \times \left(\frac{8.2+7.1}{2}\right) = 229.5$

(4) $(120-90) \times \left(\frac{7.1+6.5}{2}\right) = 204$

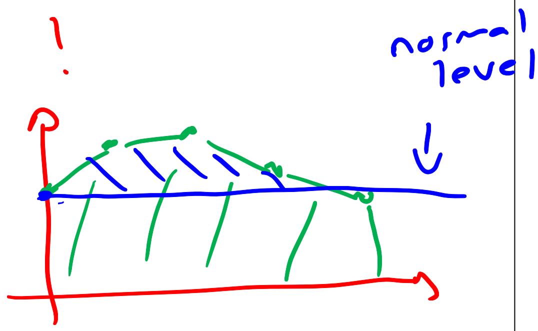
879 $\frac{mmol}{L}$ min

***Question** 10.2.1 (continued)*

(c) The paper [24] found that the "glucose AUC" for the control group is around 265 mmol/L/min. Comment on the units and compare the given AUC for the control group with your values in Parts (a) and (b).

we found 879 $\frac{mmol}{L}$ min ??

Units not correct !



265 $\frac{mmol}{L}$ min

is AUC above normal levels.

(d) How does the concept of measuring the AUC for a blood glucose curve relate to the concept of *total exposure to alcohol* discussed earlier.

Blood glucose AUC is calculated relative to a normal level ~ 5 $\frac{mmol}{L}$

Blood alcohol AUC is calculated relative to normal ~ 0

End of Case Study 22: Sweet P's.