Researchers in Schools

Life, Death and Equations, Can Maths Save Your Life?

Key Stage 4 Programme

Pupil Name

Coursebook Designed by **Dr. Niall McInerney**

Timetable and Assignment Submission

Timetable – Tutorials

Tutorial	Date	Time	Location
1 (Launch Trip)	Dec 2nd, 2019	13:00	University of London
2	December 9th, 2019	15:20-16:20	Debden Park F42
3	December 16th, 2019	15:20-16:20	Debden Park F42
4	January 20th, 2020	15:20-16:20	Debden Park F42
5	January 27th, 2019	15:20-16:20	Debden Park F42
6 (Feedback)	February 3rd, 2019	15:20-16:20	Debden Park F42
7 (Feedback)	February 10th, 2019	15:20-16:20	Debden Park F42

Timetable – Homework Assignments

Homework Assignment	Description	Due Date
Tutorial 1	Baseline Assignment	December 9th
Tutorial 2	Assignment 2	December 16th
Tutorial 3	Assignment 3	January 20th
Tutorial 4	Assignment 4	January 27th
Tutorial 5	Final Assignment	February 3rd

Assignment Submission – Lateness and Plagiarism

Lateness	
Submission after midnight on March 6th	10 marks deducted
Plagiarism	
Some plagiarism	10 marks deducted
Moderate plagiarism	20 marks deducted
Extreme plagiarism	Automatic fail

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Course Rationale

Have you ever wondered why you can only take painkillers 4 times a day? What happens when we stray from these recommended dosages? Wouldn't it be easier for you to take one pill per headache? This course looks at these questions using mathematics, introducing a real-world example of its power in the design of our medicines and medical devices, and how complicated systems of equations are shaping the future of our healthcare.

In this course, we will first discuss traditional medicine delivery methods and their advantages and disadvantages, as well as some important design considerations. The concept of mathematical modelling will be introduced, where a real-world problem is translated into mathematical language and solved, followed by the interpretation of this solution in the context of the original problem posed. A number of interesting examples will be explored (weather prediction, space exploration, Google search engines), before focussing in more detail on the controlled release of drugs from modern drug delivery methods. The motivation for studying these problems from both the perspective of mathematicians and the pharmaceutical industry will be explored. The links between these complicated systems and the mathematics learned in school (KS3 and KS4) will be examined.

The primary aims of this course are to study how interlinked mathematics and medicine have become and why it is important that these links are fostered, and to examine the real world relevance of the mathematical skills taught in school. 50% of the content will be on the application, and 50% on the relevant mathematical tools needed. The final assessment will reflect these aims, requiring you to produce a researched report on why mathematical modelling is a useful tool in the pharmaceutical industry, and its potential to guide further breakthroughs in the future. You will also be required to complete a set of mathematical problems based on the material studied in the tutorials.

Uni Pathways Mark Scheme 2019 – problem-set assignments

	Skills	1st (70-100)	2:1 (60-69)	2:2 (50-59)	3rd (40-49)	Mark /100
Subject knowledge	Knowledge and understanding	○ All content included and materials used are relevant to the general topic and to the specific question/title ○ Good understanding of all the relevant topics. ○ Technical terms are defined and used accurately throughout ○ Clear justification of how the material and content included is related to the specific issues that are the focus of the assignment	○ Most of the content included is relevant to the general topic and to the specific question/title ○ Good understanding of most the relevant topics ○ Technical terms are used accurately but not always clearly defined. ○ Adequate justification of how the content included is related to the specific issues that are the focus of the assignment	○ Some of the content included is relevant to the general topic and to the specific question/title ○ Good understanding on some of the relevant topics but occasional confusion on others. ○ Scientific terms are used mostly accurately with occasional confusion and often not defined. ○ Some justification on how the content included is related to the specific issues that are the focus of the assignment	○ The content included and materials used are not applied to the question/title in a relevant manner ○ There is confusion in how understanding of the topics is expressed	
Critical thinking	Research and evidence	○ Uses evidence/calculations to support claims/assertions/ideas, consistently clearly and convincingly ○ Data is effectively analysed, and appropriate assumptions/conclusions are reached	○ Uses evidence/calculations to support claims/assertions/ideas, mostly clearly and convincingly ○ Data is analysed and the assumptions/conclusions that are reached are mostly appropriate	○ Uses evidence/calculations to support claims/assertions/ideas, at times clearly and convincingly ○ There is an attempt to analyse data is and draw assumptions/conclusions	○ Data is presented largely without analysis	
	Developing an argument	○ Argument/proof is <u>exceptionally</u> well-developed and well-justified ○ Uses content from the tutorials in an unfamiliar context and does so accurately and confidently.	○ Argument/proof is <u>clear and well-developed,</u> and position is justified ○ Uses some content from the tutorials in an unfamiliar context, but not always accurately	○ Argument/proof is <u>clear but not well-developed</u> ○ Limited use of content from the tutorials in other contexts	○ Sometimes the argument/proof is not clearly established ○ Limited use of content from the tutorial and often inaccurately	
	Critical evaluation	○ Effectively critiques the problem set and effectively establishes a thorough response to it	○ Some evidence of critiquing the problem set and establishes a reasonable response to it	○ Limited evidence of critiquing the problem set and establishes a response to it that has some coherence	○ The problem is explored in the work but without explanation	
Wri tte	Structure and presentation	○ Ideas are presented in paragraphs and arranged in a logical structure that is appropriate for the	○ Ideas are presented in paragraphs and arranged in a structure that is mostly appropriate for the	○ Ideas are presented in paragraphs and arranged in a structure ○ The introduction mentions how the	○ Ideas are presented in paragraphs but there is a lack of structure in	

		assignment ○ The introduction clearly outlines how the essay/report will deal with the issues ○ The conclusion summarises all the main points clearly and concisely ○ All calculations, formulas and methods are clearly structured, clear to follow and correct ○ Tables and graphs are effectively constructed including appropriate headings, units and scales. ○ All sources are referenced correctly in an agreed format	assignment ○ The introduction adequately describes how the essay/report will deal with the issues ○ The conclusion summarises most of the main points clearly ○ Calculations, formulas and methods are mostly structured, clear to follow and correct ○ Most tables and graphs are well constructed ○ Most sources are referenced correctly in an agreed format	essay/report will deal with the issues ○ The conclusion summarises some of the main points clearly ○ Calculations, formulas and methods are not always structured, clear to follow and correct. ○ Some tables and graphs are well constructed but contains some errors ○ Some sources are referenced correctly in the agreed format with occasional errors	how the work is presented ○ The work lacks an introduction that establishes the scope of the question ○ The work lacks a conclusion that summarise the main points raised ○ Work is not referenced accurately	
	Language and style	○ No spelling, grammar or punctuation errors ○ Writing style consistently clear, tone appropriate and easy to follow ○ Accurate and consistent use of technical language and vocabulary	○ Minimal spelling, grammar or punctuation errors ○ Writing style mostly clear, tone appropriate and easy to follow ○ Some attempts of using technical language and vocab alary, but not always accurate	○ Some spelling, grammar or punctuation errors ○ Writing style moderately clear, tone appropriate and easy to follow ○ Use of simple language and vocabulary effectively but struggles to use technical language	○ There are a significant number of spelling, grammar and punctuation errors ○ Use of simple language and vocabulary effectively but a lack of technical language	

Overall Mark for written element (average of the 6 marks from the criteria above)/100	
	+
Problem Set mark/100	
	÷ 2
Final mark/100	

Baseline Assignment (problem-set): Pupil Feedback Report

Name of Pupil	
Name of School	Debden Park High School
Name of RIS teacher	Dr McInerney
Title of Assignment	Traditional drug delivery methods

How your assignment is graded:

Grade	Marks	What this means
1st	70+	Performing to an excellent standard at A-level
2:1	60-69	Performing to a good standard at A-level
2:2	50-59	Performing to an excellent standard at GCSE
3rd	40-49	Performing to a good standard at GCSE
Working towards a pass	0-39	Performing below a good standard at GCSE
Did not submit	DNS	No assignment received by The Brilliant Club

Lateness	
Any lateness	10 marks deducted
Plagiarism	
Some plagiarism	10 marks deducted
Moderate plagiarism	20 marks deducted
Extreme plagiarism	Automatic fail

Marks

OVERALL MARK / 100		FINAL MARK / 100 (including any deductions)	
DEDUCTED MARKS		FINAL GRADE	

If marks have been deducted (e.g. late submission, plagiarism) the teacher should give an explanation in this section:

Mark Breakdown and Feedback

Knowledge and Understanding		Research and Evidence	
	mark		*mark*
Developing an Argument		**Critical Evaluation**	
	mark		*mark*
Structure and Presentation		**Language and Style**	
	mark		*mark*

Problem Set	
Comment	*mark*

Final Assignment (problem-set): Pupil Feedback Report

Name of Pupil	
Name of School	Debden Park High School
Name of RIS teacher	Dr McInerney
Title of Assignment	The Future of Drug Delivery

How your assignment is graded:

Grade	Marks	What this means
1st	70+	Performing to an excellent standard at A-level
2:1	60-69	Performing to a good standard at A-level
2:2	50-59	Performing to an excellent standard at GCSE
3rd	40-49	Performing to a good standard at GCSE
Working towards a pass	0-39	Performing below a good standard at GCSE
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Marks

OVERALL MARK / 100		FINAL MARK / 100 (including any deductions)	
DEDUCTED MARKS		FINAL GRADE	

If marks have been deducted (e.g. late submission, plagiarism) the teacher should give an explanation in this section:

Mark Breakdown and Feedback

Knowledge and Understanding		Research and Evidence	
	mark		*mark*
Developing an Argument		**Critical Evaluation**	
	mark		*mark*
Structure and Presentation		**Language and Style**	
	mark		*mark*
Problem Set			
			mark

Subject Vocabulary

Word	Definition	In a sentence
Concentration	The relative amount of a substance in a volume.	The concentration of Robinsons in my drink was too high and made it disgusting.
Dissolve	When a substance breaks up into its smaller components to become part of a liquid.	I could no longer see the sugar in my tea after it had dissolved.
Diffusion	The movement of anything from a region of high concentration to low concentration.	The stink of smelly feet diffused around the room until it was unbearable.
Controlled Release	When medicine is delivered slowly and in a predictable fashion.	The safety and effectiveness in controlled release medicines is far higher than in traditional ones.
Polymer	A material that is made up of long repeating sub-units.	Nylon, polystyrene, DNA, silicone and silly putty are all examples of polymers.
Invasive/non invasive	Any medical procedure where skin must be broken/ or not.	Brain surgery is an invasive procedure but taking a painkiller is non invasive.
Model	A representation of an idea or system, often described in mathematical language.	Charles Darwin proposed a model of human evolution.
Analytic solution	An exact solution to a mathematical problem that can often be found using pen and paper.	The linear equation $2x + 1 = 7x$ has the analytic solution, $x = \frac{1}{5}$.
Numerical solution	An approximate solution normally called upon if an analytic solution is not possible.	The equation $\sin(x) + x + 1 = 0$ has no analytic solution but has numerical solution $x \approx -0.5$.
Calculus	Mathematics that involves the study of rates of change.	Calculus is impossible to catch as it's always on the move.

Tutorial 1 – Maths in the Real World

Objectives

- Discuss and brainstorm some applications of mathematics in the real world
- Revise the interpretation of graphical data.

TASK 1: Maths is useful 1

- In groups of three, list some reasons for why you think maths is useful in the following contexts.

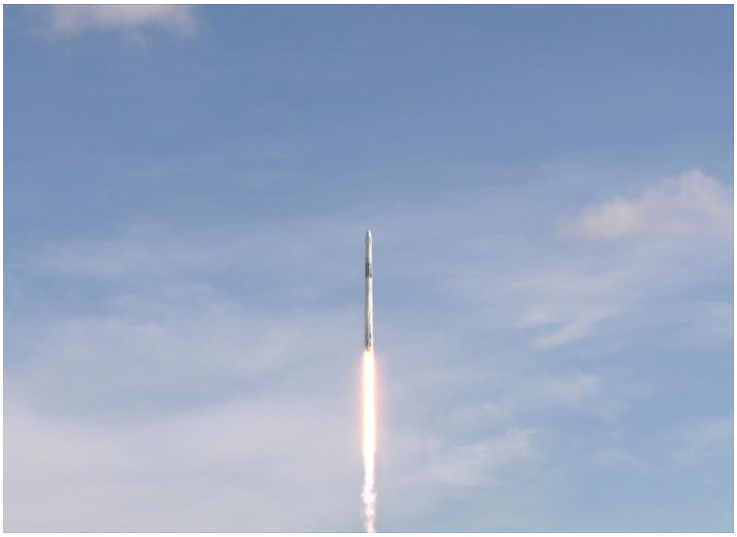
A) Google's Page Rank Algorithm

NOTES:

B) Climate Change

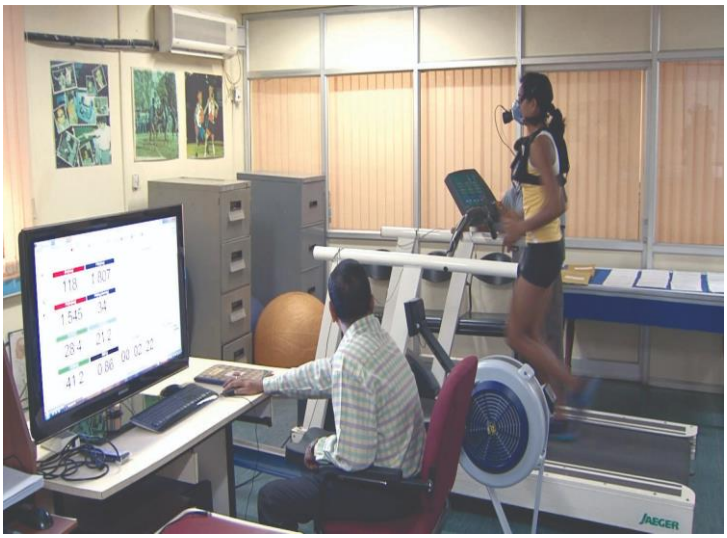
NOTES:

C) Space Travel



NOTES:

D) Sport Science



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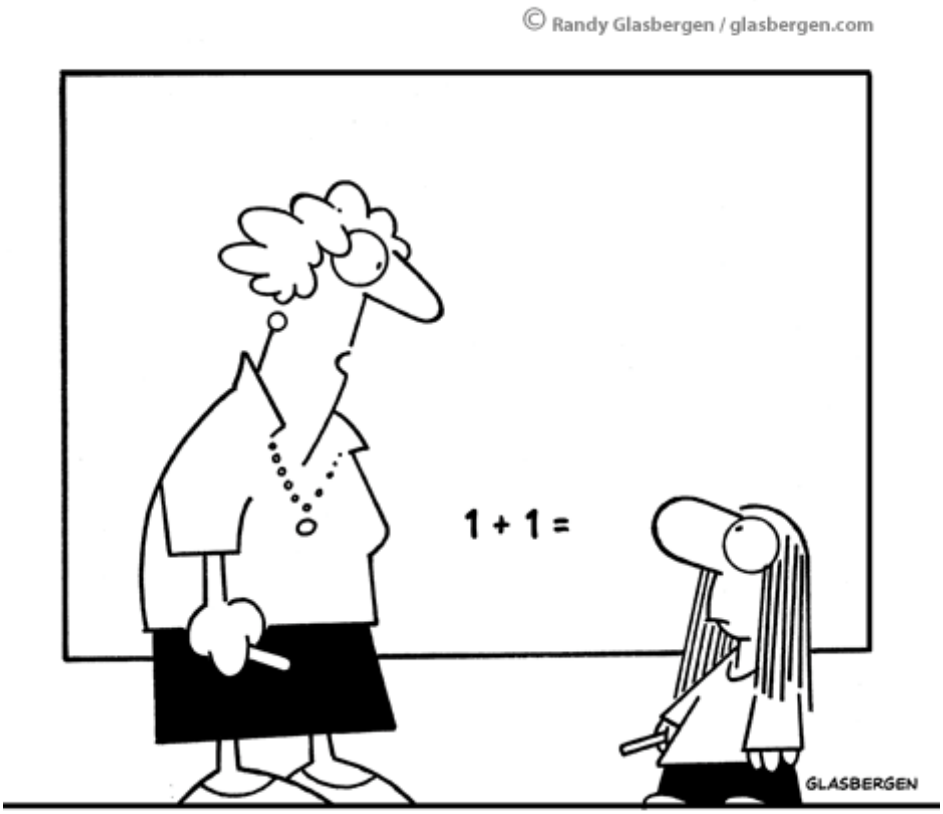
TASK 2: Maths is useful 2

- In pairs, come up with three other industries that you think Maths is important to, and explain your answer.

What scientific, engineering or industrial application is maths useful for?	Explain your answer

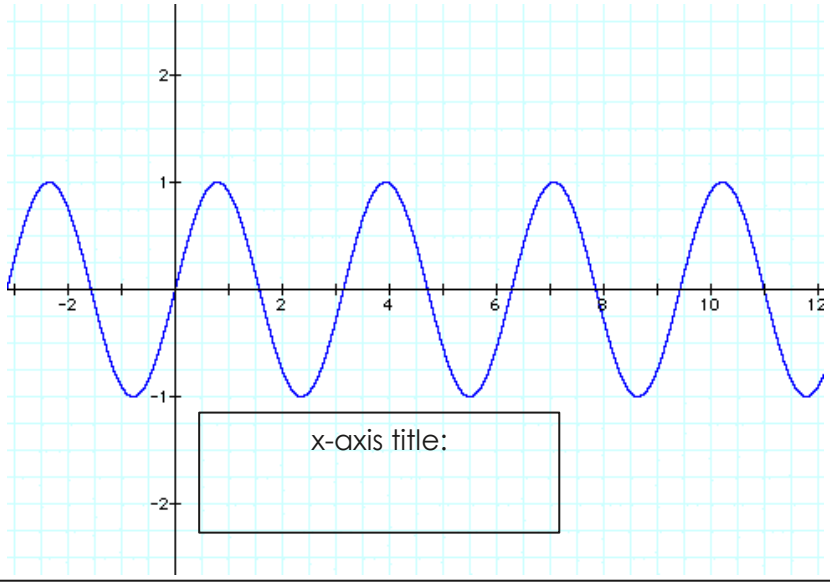


"Yes, this will be useful to you later in life."

TASK 3: Interpreting graphs

- For the following two graphs, insert axes titles and justify your answers.

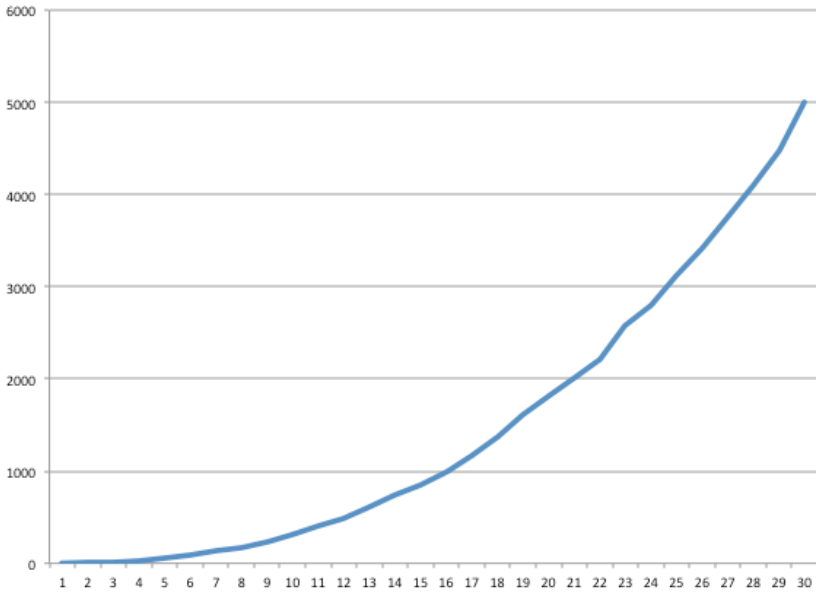
y-axis title:



x-axis title:

Explain your answer:

y-axis title:



x-axis title:

Explain your answer:

BASELINE ASSIGNMENT

Baseline assignment title: Mathematics in the real world: where are we now?

Baseline assignment instructions:

1- Write a report (250 words minimum) on the use of mathematics in a scientific, engineering or industrial context. Your examples can include expansions on those discussed in tutorial 1, but preferably will be new, well-researched examples. (50%)

2 – Solve a problem sheet with 10 questions on linear algebra, scatter plots, reading graphs. (50%)

Baseline assignment success criteria:

1- Your report should use and expand on the keywords introduced in tutorial 1, and feature appropriate sources that are referenced (SEE APPENDIX 1). Consider using the PEE (Point, Evidence, Explanation) structure when composing your essay. (STRUCTURE AND PRESENTATION, PROOFREAD)

2- Correct solutions to all problems should be displayed in a clear style and show all logical steps to the answer. When graphing a function, label both the axes AND the function.

THE BASELINE ASSIGNMENT ESSAY SHOULD EITHER BE HANDWRITTEN OR TYPED USING MICROSOFT WORD, FEEL FREE TO USE THE BOX BELOW TO BRAINSTORM SOME IDEAS FOR YOUR ESSAY.

IDEAS

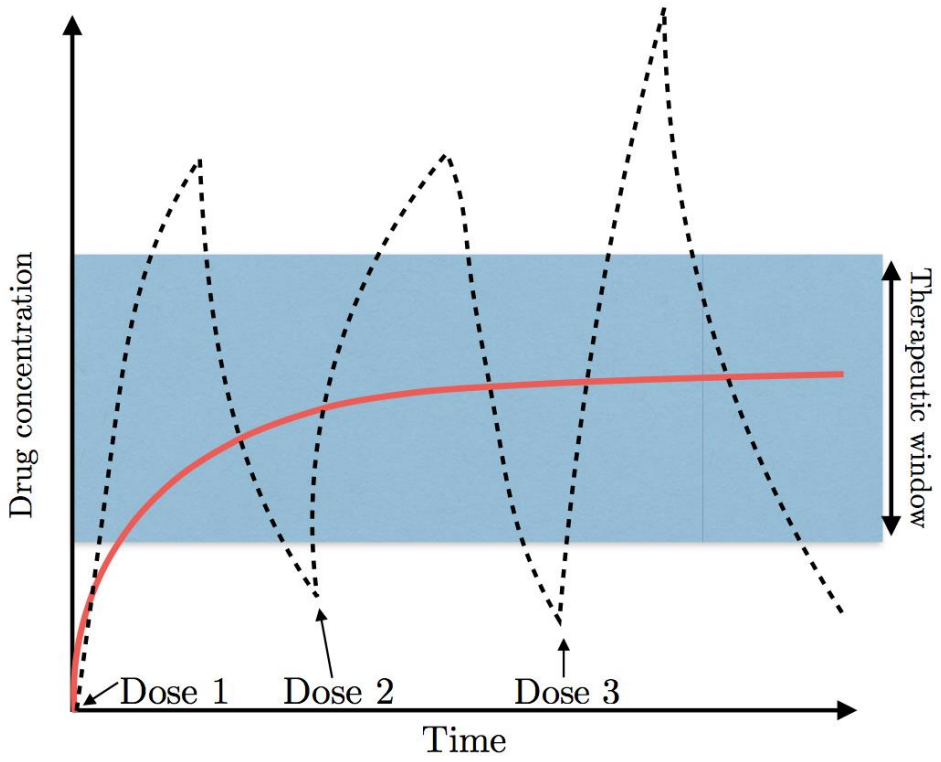
Tutorial 2 – Drug Delivery Devices

Objectives

- Introduce drug delivery devices, and considerations when designing new medicines
- Solve and plot linear equations

The primary objective of drug delivery devices is to deliver a drug at a rate determined by the needs of the body over a specified period. It is crucial to control the speed at which the drug is released; too much can be harmful to the body, but too little may limit its effectiveness. This is illustrated using the concept of a therapeutic window, where a minimum concentration is required for the drug to be effective and too much of the drug can lead to levels above a toxic threshold.

To improve the performance of drug delivery systems, traditional delivery methods are frequently replaced by controlled release systems, and mathematical modelling has the potential to be a significant tool in facilitating product development in the pharmaceutical industry. Modelling can significantly assist in the design of drug delivery systems in determining the appropriate geometry, dimensions and composition of a system, as well as the initial drug loading concentration.



TASK 1: Considerations when designing new medicine

Class brainstorm: what considerations are important when designing new medicine and medical devices?

NOTES:

TASK 2: Traditional drug dosage forms

In pairs: list as many traditional ways that medicine is delivered to the body

How is the drug administered?	Advantages/Disadvantages	Example of when this method would be used.
Pills/ Capsules / Suppositories		
		Skin rash, Localised, non-invasive, VERY slow
	Fast acting and non-invasive.	

TASK 3: Linear equations

Individually, on the following coordinate grid, sketch the lines,

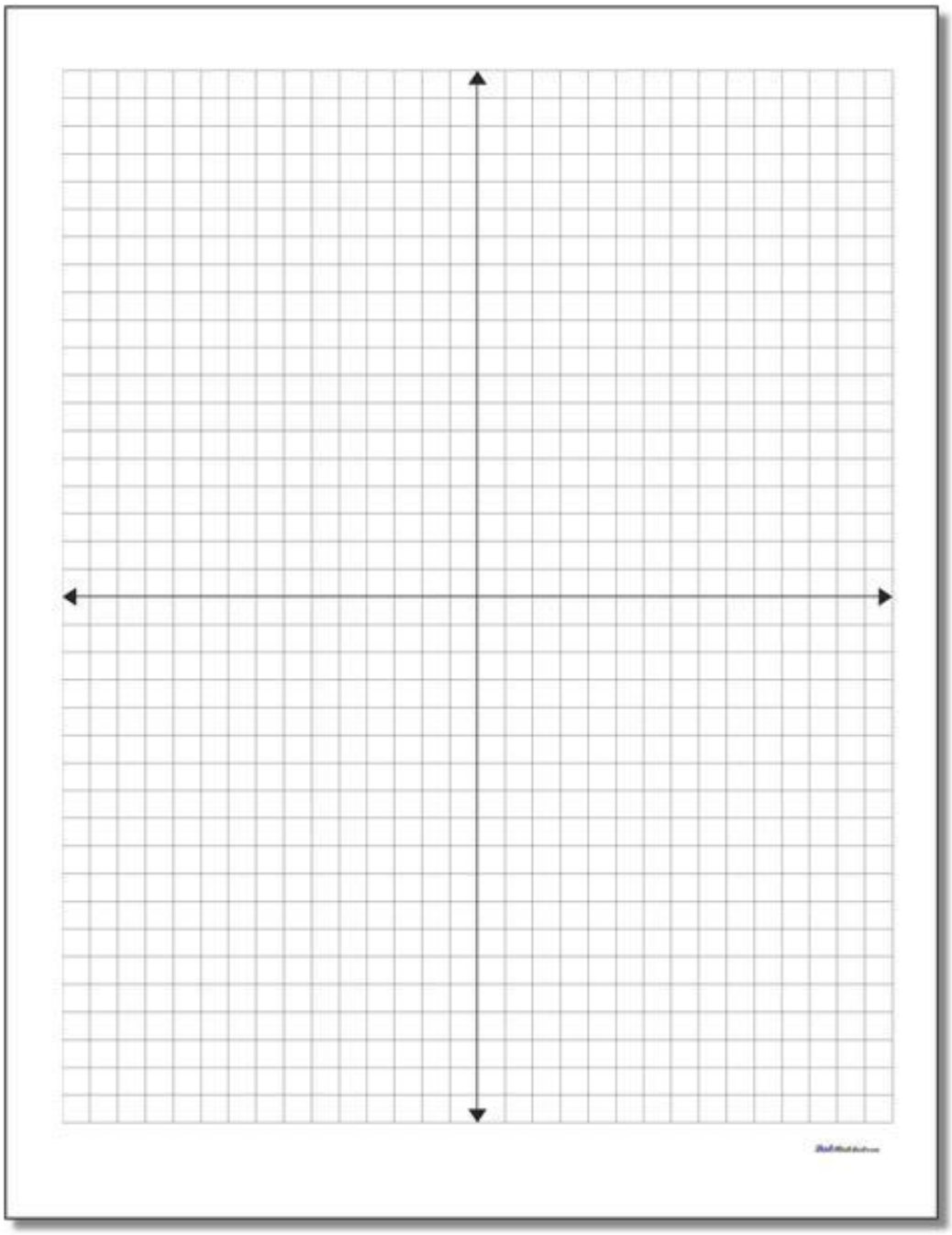
A) $y = x$

B) $y = 2x + 1$

C) $y = -x + 4$

EXTENSION 1: What is the equation of a line that passes through the point (-1,-1) and has a slope of 3.

EXTENSION 2: Write and sketch the equations of the lines that are perpendicular to lines A) B) and C).

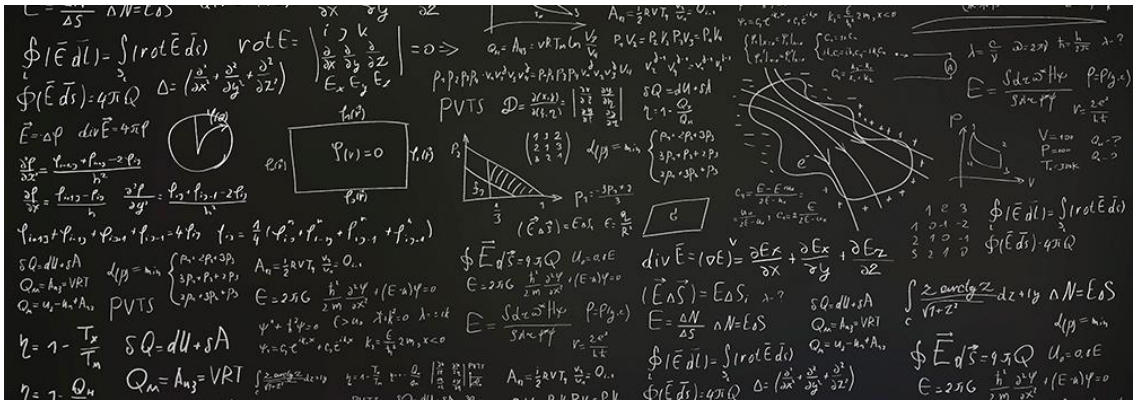


HOMEWORK: COMIC STRIP LINEAR EQUATIONS!

Tutorial 3 – What is Mathematical Modelling?

Objectives

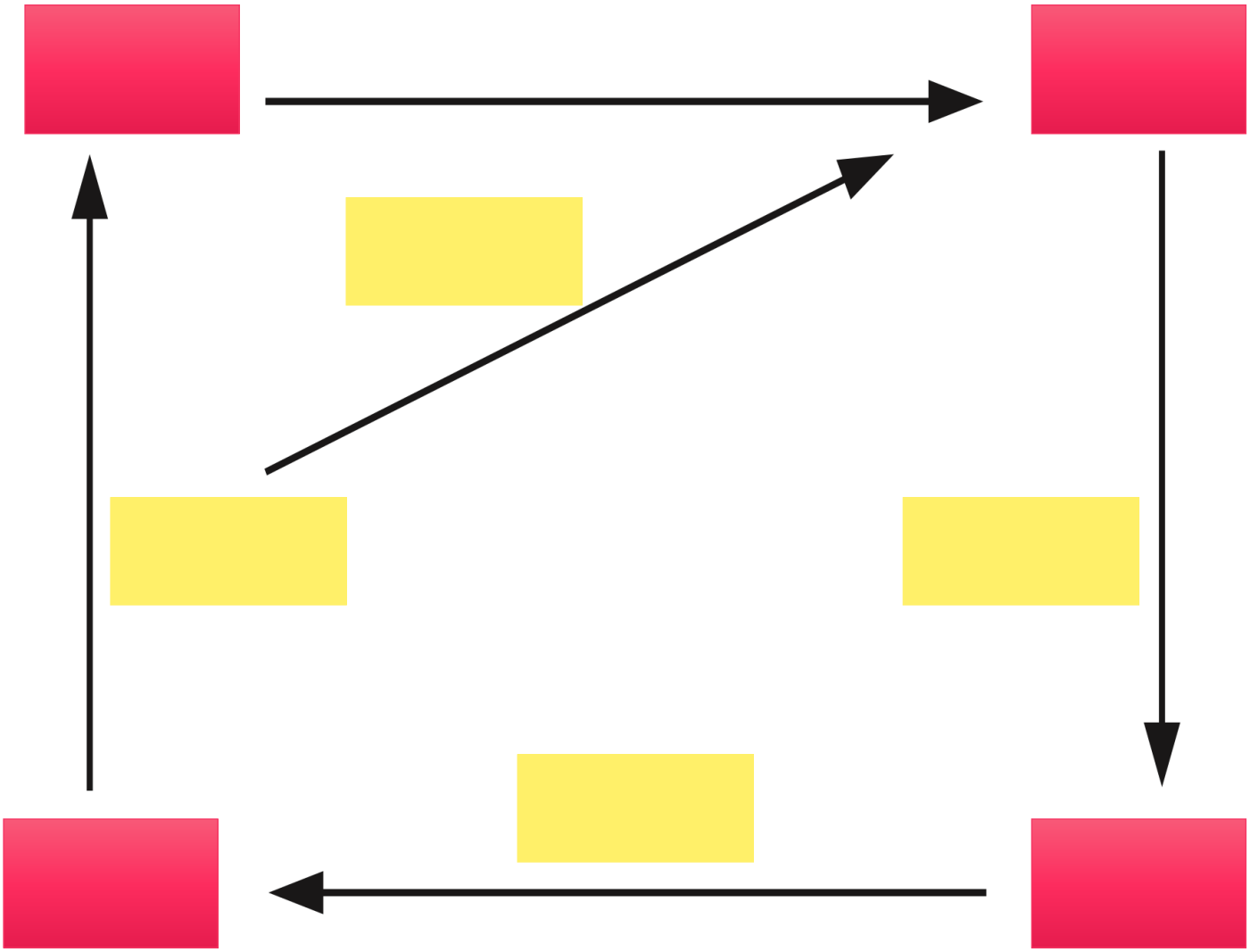
- Introduce the concept of mathematical modelling and smart drug delivery devices
- Review lines of best fit and why they are useful for medicine design



TASK 1: Flowchart of Mathematical Modelling

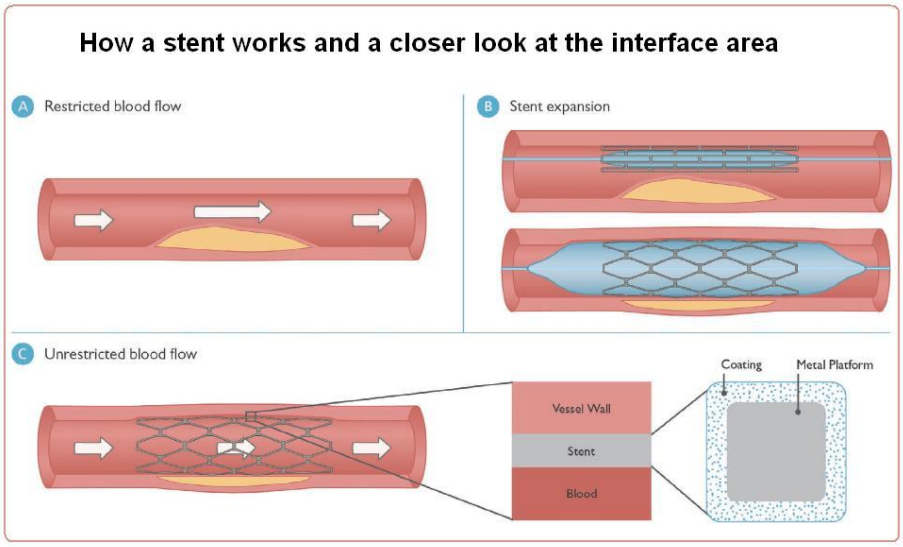
In groups of 3, try and fit the correct terms in the different locations of the flow chart.

Yellow Terms: analyse, improve, predict, interpret.
Red Terms: mathematical solution, real world problem, result, mathematical model.



Smart Drug Delivery Devices

Drug releasing stents



Notes

Hydrogels

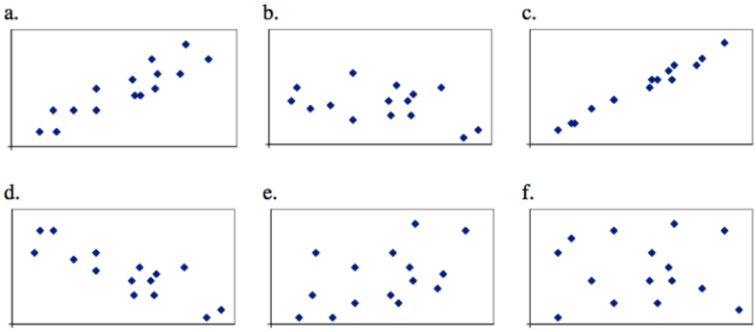
Notes

TASK 2: Lines of best fit

1) A linear model for predicting prize winnings at a race is based on data for 3 years. Do you think the model would be accurate or inaccurate? Why?

2) What does it mean to say that data has a strong negative correlation?

3) Match each correlation coefficient to a scatterplot and state whether it's a good linear model or not. Then draw a line of best fit, if appropriate.



$r = -0.85$

$r = -0.40$

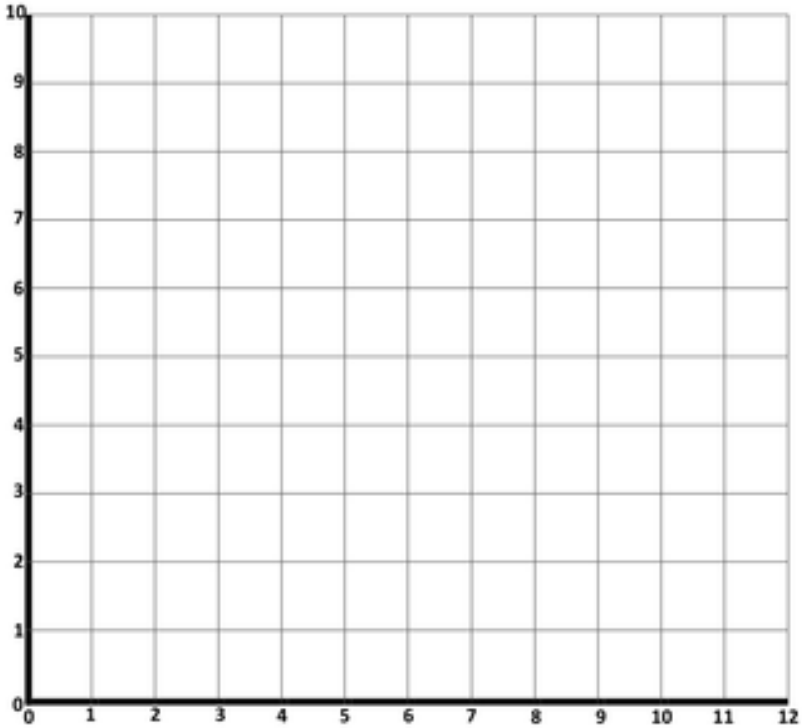
$r = 0$

$r = 0.50$

$r = 0.90$

$r = 0.99$

4) Sketch the graph of a scatterplot that has a correlation coefficient of exactly 1, but the slope of the line of best fit is greater than 1.



Tutorial 4 – Building mathematical models

Objectives

- Practice the art of mathematical modelling
- Learn to engage with academic literature

TASK 1: Building a model- snowman problem

After the first big snow of winter, a group of children gathered to build a snowman. The snowman was composed of three spherical shaped snowballs. Upon completion, the children went home for lunch and returned to the snowman one hour later only to find that he was quickly melting under the warm sun. Figure A is a picture of the snowman just after being built, and Figure B is a picture of him one hour later. For each figure, the scale is 1 cm = 30 cm.

Figure A

Figure B

(a) Estimate the volume (in cm^3) of the snowman's body just after he was built (Figure A). Show calculations that lead to your answer.

(b) Estimate the volume (in cm^3) of the snowman's body after one hour has elapsed (Figure B). Show calculations that lead to your answer.

(c) Using the volumes from (a) and (b), calculate the percent decrease of the volume after one hour.

(d) Using the percent decrease from (c), complete the table below.

t (hr)	0	1	2	3	4	5
V (cm^3)						

(e) Using the volume from the table above, estimate the radius of each snowball after 5 hours. Show calculations that lead to your answers.

(f) Assuming that the percent decrease of the volume remains constant, determine the approximate time required for the snowman to melt completely.

Rough work (Snowman Problem)

Task 2: Constant-Rate Disease Model

Often, when modelling real-world phenomena, we are interested in forecasting future values. That is, we want to explore how the value of something we care about changes over time. We will discuss several approaches that we could take to find a solution to the constant-rate disease model (in which we want to determine the number of people who are infected with a disease under the assumption that each person afflicted with a disease spreads it to exactly r people over a given time period t). For this example, we'll let I= 10, t = 2 days, and r = 5. In other words, we have a situation in which 10 people were infected with a disease that they, and all other future individuals who become infected, will each transmit to exactly 5 susceptible individuals every 2 days.

1- How many people will be diseased after 2 days?
2- How many people will be diseased after 10 days?
3- How many people will be diseased after n days?
4- Graph the data appropriately.

Rough work (Disease Spreading Problem)

Rough work (Disease Spreading Problem)

TASK 3: Engaging with academic literature: Modern drug delivery methods

Reading Strategy
The SQ3R Method

- **Survey**, skim, and scan entire reading assignment. Observe titles, subtitles, charts, diagrams, figures, tables. Preview the conclusion and summary and then the abstract/introduction. Think of this step as a "preview" to a movie you are about to watch.
- **Question** the authors' purpose and tone. Develop and write out questions about each section of the reading. You'll want to find the answers as you engage in the reading. Use these questions to guide your reading and your note-taking process.
- **Read** the assignment as thoroughly as possible. Read one section at a time, reflect on what you read, and don't get too bogged down with details. Search for the main ideas and supporting details. Keep reading!
- **Recite** and recall the information by summarizing and paraphrasing. Did you find the answers to the questions you wrote down earlier?
- **Review** the reading again and over time.

Read the following introductory extract and answer the comprehension questions that follow.

Contents lists available at ScienceDirect

Mathematical Biosciences

journal homepage: www.elsevier.com/locate/mbs

A decade of modelling drug release from arterial stents

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ARTICLE INFO

Article history:
Available online 9 July 2014

Keywords:
Mathematical modelling
Drug-eluting stents
Drug delivery
Drug release
Binding
Biological tissue

ABSTRACT

Drug-eluting stents have revolutionised the treatment of coronary artery disease. These small medical devices have attracted much interest over the past decade from biologists, clinicians, engineers and mathematicians alike. This article provides a comprehensive review of the modelling of drug release from arterial stents and the subsequent drug transport through arterial tissue, and acts as a useful reference equally for those who are already involved in drug-eluting stents research and for those who are starting out in the field. Assembled in this review are the main models of drug release and arterial drug transport that have been published in the literature to date. Many of the models presented in this paper have evolved from drug transport models in other applications. Furthermore, the ideas presented in this review may also be extended to other drug-delivery applications, such as drug coated balloons, transdermal patches and therapeutic contact lenses.

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1. Introduction and Background

Arterial stents have revolutionised the treatment of coronary heart disease (CHD). Acting as a supporting scaffold, these small mesh devices are now routinely inserted into arteries where the blood flow has become dangerously restricted (see Fig. 1). There are many benefits to the patient over more traditional treatment strategies such as open-heart surgery, including a lower incidence of major complications and an expedited recovery time. Furthermore, most patients do not require general anesthesia. Over the past decade, arterial stents have evolved from mere bare metal scaffolds to polymer coated drug-delivery vehicles and, more recently, sophisticated fully biodegradable drug delivery configurations. The driver behind these continuing advances is the desire to improve clinical outcomes. The original bare metal stents, while revolutionary at the time, were soon rendered unsatisfactory due to the relatively quick occurrence of restenosis, the re-narrowing of the lumen. The next wave of arterial stents included a drug designed to prevent the occurrence of restenosis: these are the so-called drug-eluting stents (DESs). The development of these stents threw up all sorts of questions such as: What type of drug should be used? How much drug should be coated on the stent? How will the drug release be controlled? Effective DES design became the priority for many of the top medical device companies, with considerable budgets spent on developing these products. In 2002 the first-generation DESs, Cypher (sirolimus-eluting stent; Cordis Corporation) and Taxus (paclitaxel-eluting stent; Boston Scientific Corporation) arrived. They comprised a stainless steel platform with a drug containing polymer coating attached to the stent struts [1,2]. The philosophy behind this design was to allow the drug to be released gradually so as to avoid toxic levels of drug initially, but also to permit sustained delivery over many weeks. The Cypher stent actually consists of multiple polymer layers designed to enhance the controlled nature of the release. The drugs used (sirolimus and paclitaxel) are both lipophilic and are able to inhibit smooth muscle cell (SMC) proliferation and migration. The second-generation DESs Endeavor (zotarolimus-eluting; Medtronic), Promus (everolimus-eluting; Boston Scientific Corporation) and Xience V (everolimus eluting; Abbott Laboratories) attempted to improve the biocompatibility and reduce the incidence of thrombosis which was associated with first-generation DES [3,4]. These stents were generally designed with thinner struts and utilised cobalt-chromium and platinum chromium platforms. A variety of multi-layer polymer combinations were used on these stents to attempt to control the release. Generally these stents have been shown to exhibit lower thrombosis rates compared with first generation DES [5]. Since the polymer coating in the earlier DES has been associated with a local vascular inflammatory reaction and potentially inducing late stent thrombosis, newer generation stents have focussed on biodegradable polymers (BioMatrix, Biosensors Inc, Nobori, Terumo, and Synergy, Boston Scientific Corporation), where the polymer carries and controls the drug release and then erodes or vanishes, and also coatings which do not contain any polymer at all (Yukon, Translumina and BioFreedom, Biosensors Inc), with the drug being contained on a modified surface of the stent. Perhaps the most sophisticated to date is the completely bioresorbable stent Absorb (Abbott

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http://dx.doi.org/10.1016/j.mbs.2014.06.016
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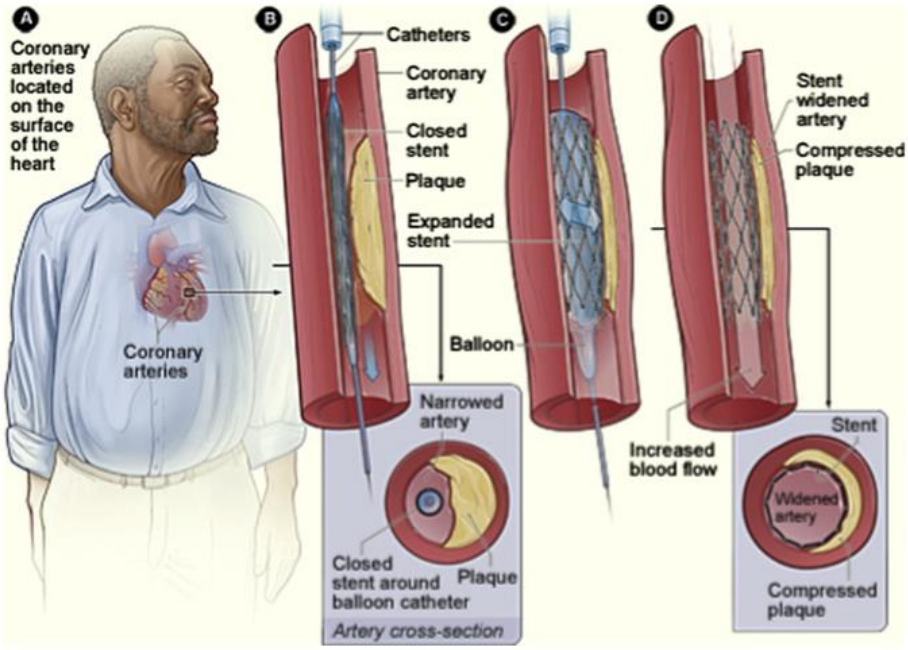


Fig. 1. Illustration of a stent being inserted at the site of a blocked artery. *Source:* National Heart, Lung and Blood Institute; National Institute of Health; U.S. Department of Health and Human Services.

Laboratories). This stent elutes everolimus in a similar way to Xience V and then resorbs naturally into the body leaving no permanent scaffold.

A significant amount of research has gone into the development of arterial stents. Countless experiments have been performed (many of which involving animals), not to mention the need for clinical trials before accreditation is finally granted. The long treacherous and costly road from a good stent design idea to regulatory approval has led many to question whether modelling could be better used to try to make this path an easier one. Indeed, only those stents which show promising results in laboratory and clinical trials are retained and those that do not are discarded – often after considerable investment. Mathematicians and engineers, realising that this complex problem is amenable to modelling, have become increasingly interested over the years. In the early years the drug release mechanism was very poorly understood, but through mathematical modelling approaches, combined with experiments, researchers have helped identify the dominant mechanisms of release in a number of stents. While release experiments alone can give information regarding the release profile and the duration of release, the data generated is for one particular set of parameters (e.g. coating thickness, drug type and concentration) and the experiment needs to be repeated for each new parameter considered. Once verified, mathematical models have the advantage of allowing several parameters to be varied and the release profiles compared without the need to repeat the experiments. The ability of a mathematical model to help identify the important parameters that govern the drug release is invaluable. Modelling can also play an important role when an understanding of the drug distribution within arterial tissue is required. Cardiologists will often stress that uniform drug concentrations across the wall are desired, and that these concentrations should be maintained within some minimum therapeutic and toxic levels. Obtaining this kind of information from experiments is extremely challenging, yet free and bound drug concentration profiles can readily be output from a mathematical model. But experiments and modelling must go hand in hand: the accuracy of the model results can only ever be as good as the quality of the inputs, especially when the model is sensitive to changes in one or more of the parameters. Indeed, the accurate determination of system parameters remains one of the biggest challenges in the field due to the natural variation between species and the complexity involved in making the required measurements, especially in the *in vivo* situation. However, some recent progress has been made by combining *in vitro*/*ex vivo* experiments with simple mathematical models, and this approach may continue to yield useful results in the future. As we shall see, the conclusions which can be drawn from modelling have provided useful insights, some of which are counter-intuitive. Among the many other benefits of adopting a modelling approach include the potential to indicate at an early stage the designs that are doomed to failure, to design stents that are optimised and to result in a reduction in the number of experiments required.

In this paper we provide a comprehensive review of the modelling of drug-release from arterial stents and the subsequent arterial drug redistribution. We firstly present the models which have been developed to describe drug release from DESs. Then, we consider how drug uptake into arterial tissue has been modelled. Thirdly, models which treat the stent and the arterial wall as a coupled system are reported. The benefits and drawbacks of each model are discussed. We have attempted to unite the various different notations in the literature. With this in mind, the models presented here may differ in notation from the original work.

2. Modelling the release of drug from arterial stents

An important aspect in the performance of any DES is the drug release profile. If too much drug is delivered then toxicity can arise, whereas if too little drug is delivered then it may have no effect at all. Of course, this "therapeutic window" varies between drugs and between patients and most probably with time after implantation too. Stent manufacturers routinely test the release of drug from their stents in an *in vitro* environment to gain an understanding of the shape of the release profile and to compare the release profile of different devices. This allows the manufacturers to ascertain the repeatability of the release profile. Whilst the *in vitro* release is

Q1- In your own words, what is a stent and why are they useful?

2- What was the problem with stent in the past, and what has been changed in their design to better accommodate the needs of the patient?

Q3- Why is mathematical modelling being used in this field of research, and what does this paper promise to add to the existing literature?

Homework: Highlight all of the words in the article that are unfamiliar to you. Do some preliminary research investigating the meaning of these words, collect formal definitions, and share them with the class at the beginning of the next lesson.

Tutorial 5 – Experimental validification

Objectives

- Discuss the value of experiments
- Engage with academic experimental research

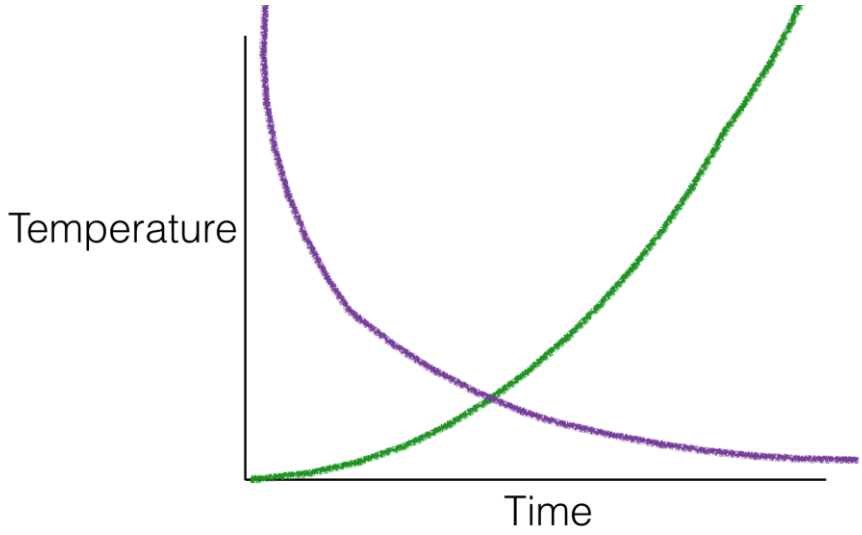
Task 1: Cooling cup of tea problem

The problem

We've all been there, you boil the water, pour it into the cup and suddenly the doorbell rings. It could be the postman, your neighbour asking for some sugar, or a religious enthusiast trying to save you from eternal damnation. Either way, it's going to be a few minutes before you can enjoy your tea. Obviously, you would like to maximise your chances of your tea still being nice and hot upon your return. What should you do? Add milk now and answer the door or pour the milk later once the nuisance business has been taken care of?

Notes

Task 2: Interpreting graphs



	What phenomenon could result in a curve like this?	What units, and range would you impose on the axes?
GREEN LINE		
PURPLE LINE		

Task 3: Pulsatile release devices, reading experimental data

Describe the behaviour of the temperature and release of drug during this experimental regime.	
How well did the researchers mathematical model explain the experimental data?	
If the experiment was carried on further, after how long would you expect 100% of the drug to release?	

Contents lists available at SciVerse ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

A mathematical model for pulsatile release: Controlled release of rhodamine B from UV-crosslinked thermoresponsive thin films

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ARTICLE INFO

Article history:
Received 9 September 2011
Received in revised form 13 February 2012
Accepted 15 February 2012
Available online 23 February 2012

Keywords:
Pulsatile release
Controllable drug delivery system
Thermoresponsive polymer
Mathematical model

ABSTRACT

A controlled drug delivery system fabricated from a thermoresponsive polymer was designed to obtain a pulsatile release profile which was triggered by altering the temperature of the dissolution medium. Two stages of release behaviour were found: fast release for a swollen state and slow (yet significant and non-negligible) release for a collapsed state. Six cycles of pulsatile release between 4 °C and 40 °C were obtained. The dosage of drug (rhodamine B) released in these cycles could be controlled to deliver approximately equal doses by altering the release time in the swollen state. However, for the first cycle, the swollen release rate was found to be large, and the release time could not be made short enough to prevent a larger dose than desired being delivered. A model was developed based on Fick's law which describes pulsatile release mathematically for the first time, and diffusion coefficients at different temperatures (including temperatures corresponding to both the fully swollen and collapsed states) were estimated by fitting the experimental data with the theoretical release profile given by this model. The effect of temperature on the diffusion coefficient was studied and it was found that in the range of the lower critical solution temperature (LCST), the diffusion coefficient increased with decreasing temperature. The model predicts that the effective lifetime of the system lies in the approximate range of 1–42 h (95% of drug released), depending on how long the system was kept at low temperature (below the LCST). Therefore this system can be used to obtain a controllable pulsatile release profile for small molecule drugs thereby enabling optimum therapeutic effects.

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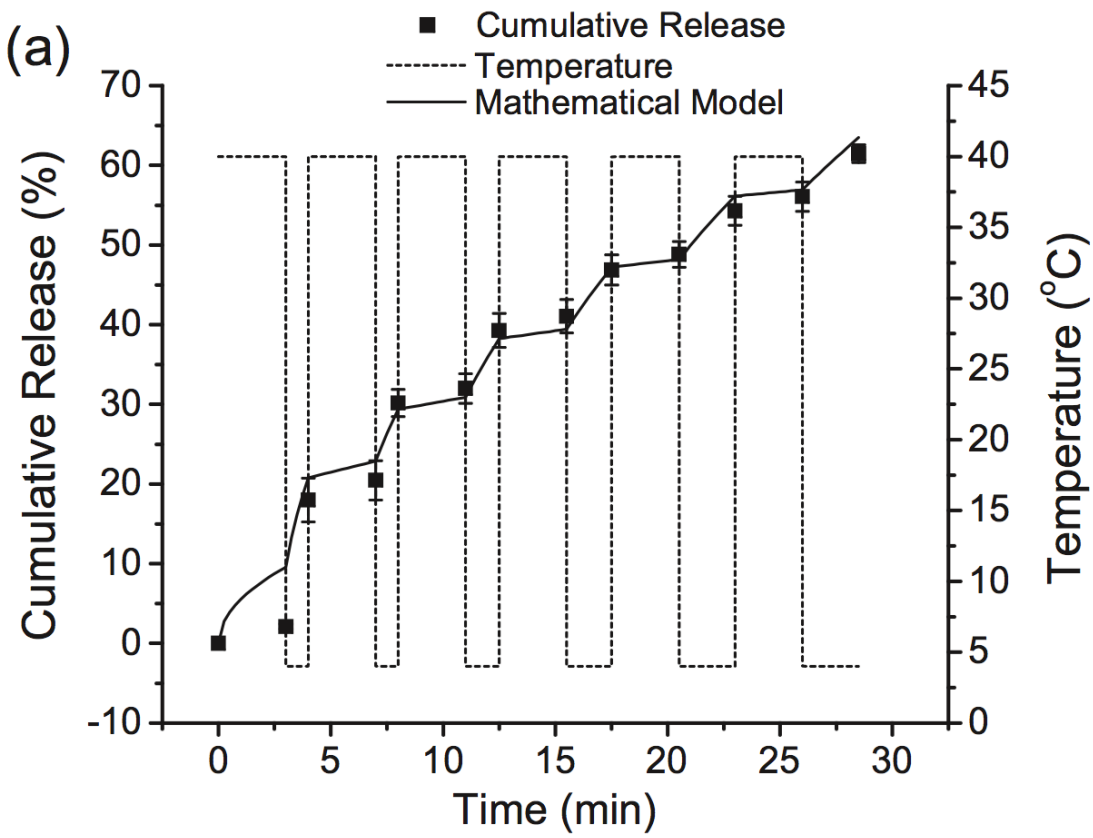

FINAL ASSIGNMENT

Final assignment title: Mathematics in the real world: where are we going?

Baseline assignment instructions:

1- Write an essay (1000 words minimum) on the use of mathematics in the real world either in a medical devices context or another relevant industry. Your examples should include expansions on those discussed in all tutorials, as well as new, well-researched examples. (50%)

2 – Solve a problem sheet with 10 questions on linear algebra, scatter plots, reading graphs. (50%)

Baseline assignment success criteria:

1- Your report should use and expand on the keywords introduced in tutorial 1, and feature appropriate sources that are referenced (SEE APPENDIX 1). Consider using the PEE (Point, Evidence, Explanation) structure when composing your essay. (STRUCTURE AND PRESENTATION, PROOFREAD)

2- Correct solutions to all problems should be displayed in a clear style and show all logical steps to the answer. When graphing a function, label both the axes AND the function.

THE FINAL ASSIGNMENT ESSAY SHOULD EITHER BE HANDWRITTEN OR TYPED USING MICROSOFT WORD, FEEL FREE TO USE THE BOX BELOW TO BRAINSTORM SOME IDEAS FOR YOUR ESSAY.

IDEAS

Tutorial 6 – Feedback tutorial

What is the Purpose of Tutorial 6?

- To receive feedback on your final assignment
- To respond to the feedback from your Uni Pathways teacher
- To write targets for improvement on your final assignment

Final assignment feedback from your Uni Pathways Teacher

(Remember to look at the mark scheme to help you understand what you have done well so far, and how you can do even better in your final assignment)

Here are three things that my Uni Pathways Teacher thought I did well in my draft assignment
•   •   •

Here are three things that my Uni Pathways Teacher thinks that I could do to get a higher mark in my final assignment
•   •   •

Tasks from my Uni Pathways Teacher to do during the feedback tutorial to help me improve
•   •   •
My response:

Actions I will take to improve my final assignment after this tutorial…
•   •   •

Hand in date for my final assignment:	

Tutorial 7 – Final tutorial

What is the Purpose of Tutorial 7?

- To receive feedback and a grade on your final assignment.
- To reflect on the programme including what you enjoyed and what was challenging.
- To ask any questions you may have about university.

Final assignment feedback from my Uni Pathways Teacher

Final mark:	University style grade:
Feedback: Here are three things that my Uni Pathways teacher thought I did well in my final assignment • • •	

Here are three things that my Uni Pathways teacher thinks I should remember for when I am doing this kind of study in the future
• • •

University

What questions do you still have about University after taking part in Uni Pathways?
• • •

Reflecting on Uni Pathways

What did you most enjoy about Uni Pathways?
• • •

What did you find challenging about the programme?	How did you overcome these challenges?
• • •	• • •

Appendix 1 – Referencing correctly

When you get to university, you will need to include references in the assignments that you write, so we would like you to start getting into the habit of referencing in your Brilliant Club assignment. This is really important, because it will help you to avoid plagiarism. Plagiarism is when you take someone else's work or ideas and pass them off as your own. Whether plagiarism is deliberate or accidental, the consequences can be severe. In order to avoid losing marks in your final assignment, or even failing, you must be careful to reference your sources correctly.

What is a reference?

A reference is just a note in your assignment which says if you have referred to or been influenced by another source such as book, website or article. For example, if you use the internet to research a particular subject, and you want to include a specific piece of information from this website, you will need to reference it.

Why should I reference?

Referencing is important in your work for the following reasons:

- It gives credit to the authors of any sources you have referred to or been influenced by.
- It supports the arguments you make in your assignments.
- It demonstrates the variety of sources you have used.
- It helps to prevent you losing marks, or failing, due to plagiarism.

When should I use a reference?

You should use a reference when you:

- Quote directly from another source.
- Summarise or rephrase another piece of work.
- Include a specific statistic or fact from a source.

How do I reference?

There are a number of different ways of referencing, and these often vary depending on what subject you are studying. The most important to thing is to be consistent. This means that you need to stick to the same system throughout your whole assignment. Here is a basic system of referencing that you can use, which consists of the following two parts:

1. **A marker in your assignment**: After you have used a reference in your assignment (you have read something and included it in your work as a quote, or re-written it your own words) you should mark this is in your text with a number, e.g. [1]. The next time you use a reference you should use the next number, e.g. [2].
2. **Bibliography**: This is just a list of the references you have used in your assignment. In the bibliography, you list your references by the numbers you have used, and include as much information as you have about the reference. The list below gives what should be included for different sources.

    a. **Websites** – Author (if possible), title of the web page, website address, [date you accessed it, in square brackets].

    E.g. Dan Snow, 'How did so many soldiers survive the trenches?', http://www.bbc.co.uk/guides/z3kgjxs#zg2dtfr [11 July 2014].

    b. **Books** – Author, date published, title of book (in italics), pages where the information came from.

    E.g. S. Dubner and S. Levitt, (2006) *Freakonomics*, 7-9.

    c. **Articles** – Author, 'title of the article' (with quotation marks), *where the article comes from* (newspaper, journal etc.), date of the article.

    E.g. Maev Kennedy, 'The lights to go out across the UK to mark First World War's centenary', Guardian, 10 July 2014.

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