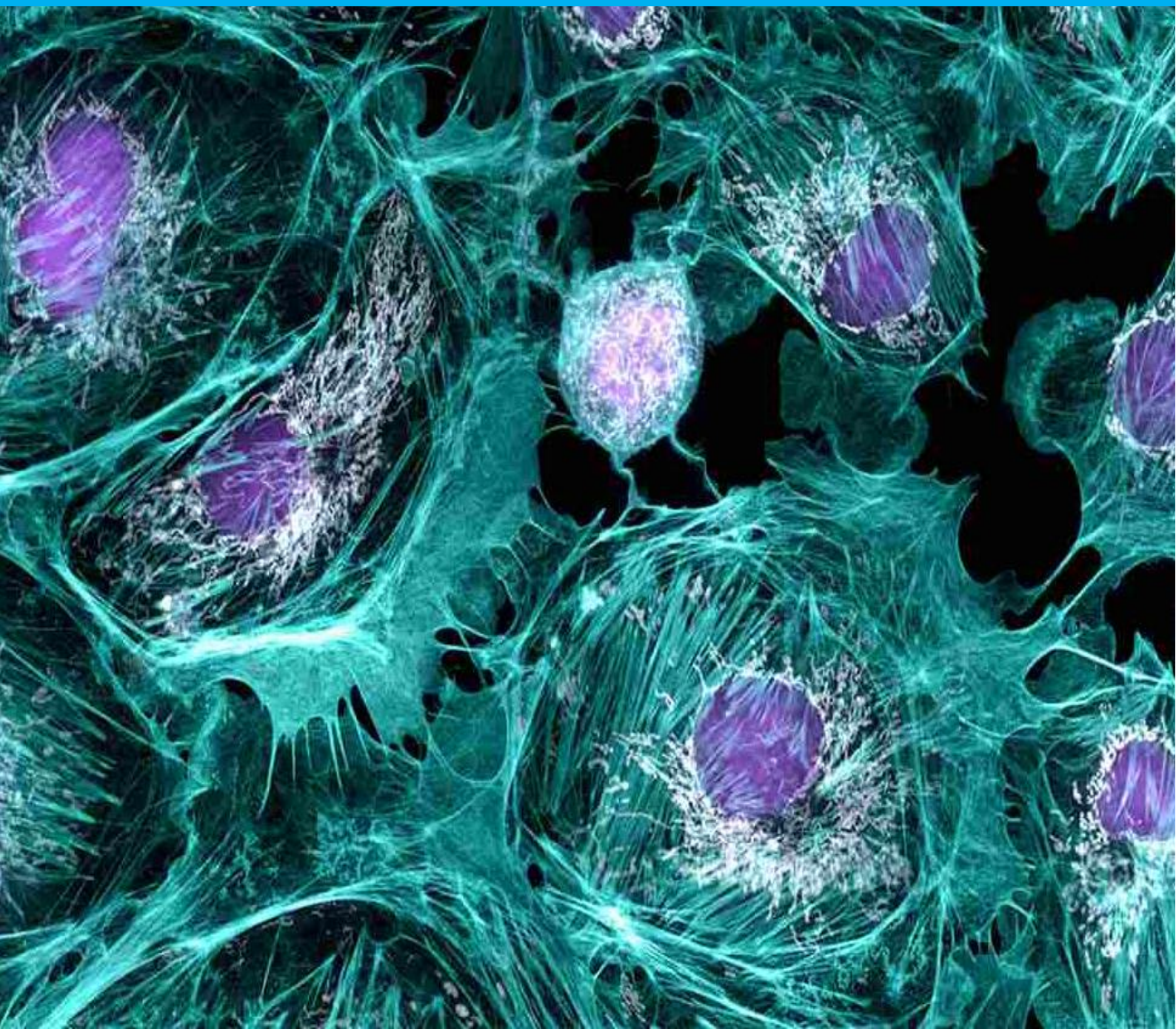
The Nanobiology Reader

Preparation for the Selection Exam of the Nanobiology Selection Procedure 2025

Nanobiology is the study of biology at its smallest scales, down to the molecular level. Like all matter, biological molecules are governed by natural laws. In our program, you learn to use physics and maths to understand and describe biology. In this manual you will get a first feeling on what it is like to study Nanobiology; how you can use the knowledge you obtained in one scientific field, to quantify a phenomenon in another.



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Introduction

Dear candidate,

Thank you for choosing to enrol into the Nanobiology program! We hope to see you at the start of the academic year.

This reading material has been composed for you as a preparation for the selection exam, the second round of the selection procedure. The exam itself consists of four parts, representing the four sciences most important to the Nanobiology program: Mathematics, Chemistry, Physics and Biology. You will be introduced to these topics in this reading material. The biology part has no written material. Instead, we ask you to watch part of a lecture of one of the first Nanobiology courses for 1st-year students, Genetics. This is an opportunity for you to get used to the lecture-based style of teaching which is applied in universities. The lecture video can be found in the section “Study material selection exam” on the Online Courses homepage and under “Documents” in the top blue bar.

In addition to this reading material, we assume that candidates who take this exam know the basics of these four sciences as taught in high school. This includes topics such as integration (including indefinite or partial), differentiation and the associated rules of calculation for Mathematics, or DNA and its replication as well as the central dogma for Biology. While there will be no explicit questions covering these concepts, we will build on them in this study material. Thus if you find this material hard to understand, please recap your knowledge.

During the exam, you are allowed to use a non-graphing calculator, pen, and scratch paper. All necessary constants will be given in the exam itself, but you do have to remember certain formulas. The formulas you are expected to know are highlighted in blue in this reader and are listed at the end. We do expect that interpretations and derivations of these formulas are also part of your skill set.

Please make sure you have read the “Manual Online Proctoring”, available on Online courses, for the do’s and don’ts while taking a proctored exam.

With this prelude, we wish you the best of luck!

With kind regards,

The Nanobiology Selection team

I. Mathematics: Differential Equations

Algebraic and Differential equations

Algebraic equations

Until now, you will have mostly worked with equations of the form

$$y = f(x)$$

A famous example is the *quadratic equation*, $y = x^2$. We can solve such an equation for x to get the expression $x = \pm\sqrt{y}$. Now, for every value y that we have, we can find the corresponding value(s) of x. We can also check our solution by inserting $x = \pm\sqrt{y}$ back into our original equation. In that case, $y = x^2 = (\pm\sqrt{y})^2 = y$. Hence our solution is indeed correct.

Often, we use *algebraic equations* such as the quadratic equation to find a certain **value** y given our information $f(x)$. We can further analyse algebraic expressions by taking their *derivative*

$$y'(x) = \frac{dy}{dx} = \frac{d}{dx}x^2 = 2x$$

or the *integral*

$$\int x^2 dx = \frac{1}{3}x^3 + C$$

with C an arbitrary mathematical constant.

Please make sure you are familiar with these concepts before you continue with the reader.

Differential equations

Often in a physical or biological context, we do not know the specific function $f(x)$ which most accurately represents our system. Rather, systems can be described by their change from one time point to the next.

Say you want to grow a strain of bacteria in your lab. You know that your strain grows by a factor of $a = 0.1$ per hour. That means that after one hour, we will have $+10\%$ more bacteria than at hour 1. We can thus write

$$\frac{dy(t)}{dt} = 0.1y(t) = ay(t)$$

where $y(t)$ is the bacterial population on any day t. That is, the number of bacteria on a certain day is dependent on the number of bacteria the previous day.

Say we now leave the agar plate with the bacteria out in the open. Then we will get a constant influx $b = 5$ of bacteria from the environment. Our equation then takes on the shape

$$\frac{dy(t)}{dt} = 0.1y(t) + 5 = ay(t) + b$$

Such an equation, which describes the relationship between an unknown function $y(t)$, its derivative(s)[1] $\frac{dy}{dt}$ and the variable of the function (e.g., t), is called a *differential equation*.

[1] While this reader will deal mostly with differential equations relying only on their first order derivative $\frac{dy}{dt}$ (fittingly called *first order differential equations*), they can also include higher order derivatives such as $\frac{d^2y}{dt^2}$, which is the derivative of the derivative.

The solution to a differential equation is a **function** $y(t)$. As an example, the solution to

$$\frac{dy}{dt} = 1.6y(t) = ay(t)$$

is

$$y(t) = Ce^{1.6t}$$

where C represents an arbitrary constant. We will look at how to find this solution in one of the sections below. This constant can usually be determined by further information we have about the system, for example the initial number of bacteria $y(0)$. We call information about the function value at $t = 0$ the *initial condition*.

Basic differential equations can be very useful when it comes to modelling systems where we have an inflow and outflow of system components, as with our growing bacterial strain. In general, such equations will have the following form:

Change in system parameter = influx - outflow

For lab-grown bacteria, we often look at the number of colonies or the number of bacteria as our *system parameters*. *Influx* then describes anything that increases this amount: population growth, bacterial influx due to contamination and the addition of new bacteria all fall in this category. Correspondingly, *outflux* then describes all occurrences that decrease the number of bacteria present, such as bacterial death or isolation (taking out) of bacteria. We can then use the model to make predictions about our system, like in this case the quantitative development of our bacterial population.

In this reader, you will be introduced to a few methods to solve certain types of differential equations.

Solving Differential Equations with a y-independent right-hand side

Arguably the simplest type of differential equations (henceforth also referred to as DEs) is

$$\frac{dy}{dx} = f(x)$$

Examples of this are equations such as

$$\frac{dy}{dx} = x^2 \qquad \frac{dy}{dx} = 5x^3 + 7 \qquad \frac{dy}{dx} = e^{3x} \qquad \frac{dy}{dx} = \frac{1}{x}.$$

What these DEs have in common is that the first derivate of $y(x)$ is described only in terms of a function of its variable, x. That is, the function $y(x)$ itself does not appear in the DE.

You might already know how to solve this type of equation! We do this by applying integration to both sides:

$$y = \int \frac{dy}{dx} dx = \int f(x) dx$$

For instance, taking

$$\frac{dy}{dx} = 5x^3 + 7$$

as our example, we can integrate

$$y = \int \frac{dy}{dx} dx = \int (5x^3 + 7)\, dx$$

to obtain

$$y(x) = \frac{5}{4}x^4 + 7x + C$$

as our solution, with C an arbitrary constant. Try taking the derivative of $y(x)$ to check for yourself that this solution is correct!

To determine the value of C, an *initial value* is needed. This additional piece of information often takes the form of $y(0) = a$. For this equation to hold, our solution must thus fulfil the requirement

$$y(0) = \frac{5}{4} \cdot 0^4 + 7 \cdot 0 + C = a$$

From this, we can deduce that $C = a$. Hence our final solution is

$$y(x) = \frac{5}{4}x^4 + 7x + a$$

For example, taking $a = 2$ this becomes

$$y(x) = \frac{5}{4}x^4 + 7x + 2$$

Initial values usually follow from physical conditions on the system we are trying to analyse. Note that we don't always have this information given when solving differential equations. In such cases, make sure to keep the arbitrary constant C in your answer, which represents the general solution for any system of this kind.

Solving separable differential equations

Another type of differential equation we can try to solve are *separable differential equations.* These equations are of the form

$$\frac{dy}{dx} = f(x)g(y)$$

That is, the derivative of $y(x)$ with respect to x is the product of two functions. One of these solely depends on x and the other depends only on y. Examples of such differential equations would be

$$\frac{dy}{dx} = (x^2 - 2)(y - 4) \qquad \frac{dy}{dx} = 6xy \qquad \frac{dy}{dx} = -16y$$

Note that the previously discussed equations written as $\frac{dy}{dx} = f(x)$ are also a type of separable differential equations, with $g(y) = 1$.

So how do we go about solving these equations? The first step in solving separable DEs is to separate the two variables, in our case y and x, by putting all terms containing y on one side of the equation, and all terms containing x on the other side of the equation. For example, we can rearrange the equation

$$\frac{dy}{dx} = (x^2 - 2)(y - 4)$$

to

$$\frac{1}{y-4}dy = (x^2-2)dx$$

Now, we can put an integration sign in front of both sides of the equality:

$$\int \frac{1}{y-4}dy = \int (x^2-2)dx$$

Note that each of the sides has to be integrated with respect to a different variable: $\int \frac{1}{y-4}dy$ is an integral with respect to y, while $\int (x^2-2)dx$ is an integral with respect to x. Remembering this, we can now do the integrations:

$$\int \frac{1}{y-4}dy = \int (x^2-2)dx$$

Which becomes

$$ln(y-4) + C_1 = \frac{1}{3}x^3 - 2x + C_2$$

The two constants can be combined into a common constant $C = C_2 - C_1$.

Now all that is left is getting an explicit expression for y . To achieve this, we must further rearrange the equation.

$$ln(y-4) = \frac{1}{3}x^3 - 2x + C \quad \leftrightarrow \quad y = Ce^{\frac{1}{3}x^3-2x} + 4$$

which is the solution to our problem.

To show this, we can take the derivative of the solution we found

$$\frac{dy}{dx} = \frac{d}{dx}Ce^{\frac{1}{3}x^3-2x} + 4 = (x^2-2)Ce^{\frac{1}{3}x^3-2x}$$

You might notice that the $Ce^{\frac{1}{3}x^3-2x}$ is very similar to our equation for y

$$y = Ce^{\frac{1}{3}x^3-2x} + 4$$

From which we can find

$$y - 4 \; = \; y = Ce^{\frac{1}{3}x^3-2x}$$

And thus, we get

$$\frac{dy}{dx} = (x^2-2)(y-4)$$

Which is indeed equal to our initial differential equation.

In general terms, the steps are as follows. For an equation of the form $\frac{dy}{dx} = f(x)g(y)$,

1. Separate the variables by rearranging the equation to $\frac{dy}{g(y)} = f(x)dx$
2. Integrate both sides: $\int \frac{dy}{g(y)} = \int f(x)dx$. When doing the integration, don't forget the integration constant C!
3. Rearrange the equation to obtain an explicit expression for y in terms of x
4. Check your answer by taking the derivative $\frac{dy}{dx}$ of your solution

Note that sometimes it is not immediately obvious from looking at a DE that it is indeed separable. For example, take a look at the following equation:

$$\frac{dy}{dx} = yx^2 - 2y - 4x^2 + 8$$

It is not immediately clear that this is a separable differential equation. However, this is actually the same as our example equation:

$$\frac{dy}{dx} = (x^2 - 2)(y - 4)$$

You can check this yourself by multiplying $x^2 - 2$ with $y - 4$. Hence, sometimes it is necessary to bring the DE into a form where the right-hand side is not expanded i.e., find out the two functions $f(x)$ and $g(x)$ which this equation is a product of. Often this can be done by isolating common factors from the terms.

Exponential Growth

There is a special subtype of separable differential equations which deserves a bit more attention, as its result is a very common and widely used expression. It models simple *growth* or *decay* and can even be used for determining the age of fossils by a method known as *carbon dating*.

The form of this DE is as follows:

$$\frac{dy}{dx} = \alpha y$$

Notice that this is a differential equation of the same form as the one we solved in the introduction to differential equations in this reader:

$$\frac{dy}{dt} = 1.6y(t) = ay(t)$$

This is a special case of separable differential equations, with $f(x) = \alpha$, which is a constant, and $g(y) = y$. Often, we will use the variables N, λ and t when writing such an equation:

$$\frac{dN}{dt} = \lambda N$$

N usually represents a quantity (of mass, objects, bacteria, radioactive material, substrate, …), t is the measure of time and λ is the *exponential growth constant.* As you might have already guessed by now, the solution to this equation is a positive exponential

$$N(t) = N_0 e^{\lambda t}$$

We will derive the result below.

Other than exponential growth, we can also have exponential decay. In that case we write

$$\frac{dN}{dt} = -\lambda N$$

and λ becomes the *exponential decay constant.* The expression for exponential decay is very similar to that for exponential growth

$$N(t) = N_0 e^{-\lambda t}$$

To solve the above equation, we proceed as usual when it comes to separable differential equations.

We start with

$$\frac{dy}{dx} = \alpha y$$

Which can be rearranged by separation of variables to get

$$\frac{dy}{y} = \alpha dx$$

The next step is to integrate both sides of this equation

$$\int \frac{dy}{y} = \int \alpha dx$$

to

$$ln(y) = \alpha x + C$$

Which, in a final step, we can rearrange to an expression for y

$$y = Ce^{\alpha x}$$

You can check for yourself that this result passes the derivative test. For exponential decay, the derivation is almost identical to that of exponential growth, except for a sign:

$$y = Ce^{-\alpha x}$$

Uses of exponential growth and decay models

Exponential growth and decay models have many uses in describing the systems around us. For example, the decay of Carbon 14 in a dead organism can be used to calculate the time of death and hence the age of many archaeological findings. Exponential decay of radioactive elements is used to predict the radiation levels we can expect to find in Chernobyl at any future timepoint (given there will not be any additional new sources of radiation), and the rate of decay of drugs in the blood system is helpful for determining the intervals at which medication should be taken.

All of this is made possible by the fact that for exponential models, the time it takes to double/halve the amount of stuff we are measuring is independent of the initial quantity present. What does this mean? Let's look at a linear and an exponential model of the breaking down of drugs in the bloodstream.

It is thought that unlike most substances, alcohol follows a linear decay model as above a certain amount of ingestion, all enzymes necessary for breaking down bacteria are occupied and thus the destruction rate of ethanol molecules cannot increase proportionally to the amount of alcohol going around in your blood. Instead, alcohol is thought to be removed at an average rate of $3.3mmolh^{-1}$, although this varies widely depending on the individual[2]. We can therefore model the rate of alcohol decline in the blood via the following differential equation:

$$\frac{dN(t)}{dt} = -3.3mmol/h$$

[2] Paton A. (2005). Alcohol in the body. *BMJ (Clinical research ed.)*, *330*(7482), 85–87. https://doi.org/10.1136/bmj.330.7482.85

whose solution is a linear equation

$$N(t) = N_0 - 3.3mmol/h \cdot t$$

where N_0 is the initial amount of alcohol molecules in $mmol$, t is the time since consumption in hours, and $N(t)$ is the number of molecules after t hours. We can now try and calculate how long it takes for the amount of alcohol to drop to half of its initial value $N(t) = \frac{N_0}{2}$

$$N(t) = \frac{N_0}{2} = N_0 - 3.3mmol/h \cdot t \leftrightarrow t = \frac{N_0}{2 \cdot 3.3mmol/h}$$

As you can see, this timeframe will always depend on the initial amount of alcohol present, and hence it is not possible for us to make a general statement on the *half-life* (the time it takes for a substance to decrease by 50%) of alcohol.

In contrast, let's consider another commonly consumed drug: caffeine. The decay of caffeine can be modelled using exponential decay with a decay constant of approximately $\lambda = 0.14$.[3]

$$\frac{dN(t)}{dt} = -0.14N(t)$$

which can be solved to produce the exponential decay model

$$\mathrm{N}(t) = N_0 e^{-0.14/h \cdot t}$$

As we did in the case of alcohol, let's look at the time it takes to arrive at $N(t) = \frac{N_0}{2}$. We get the expression

$$N(t) = \frac{N_0}{2} = N_0 e^{-0.14/h \cdot t} \leftrightarrow t = -ln\left(\frac{1}{2}\right) \cdot \frac{1}{0.14/h} = \frac{ln(2)}{0.14/h} \approx 5h$$

From this, we see that the half-life of caffeine does not depend on our initial value N_0 as in the case of alcohol. This is a crucial property of exponential decay models and stems from the fact that the rate of decay (or growth) is proportional to the amount of stuff present, unlike the constant rate we saw for alcohol above.

The fact that the half-life is independent of the initial value is a often utilized to characterize and/or describe the decay of radioactive elements and drugs. We also use the *duplication time* (the time until $N(t) = 2N_0$) for growth of bacterial populations. The half-life can also be used interchangeably with λ, as one value can be extrapolated from the other via rearranging the model equation to give the required parameter (as we did above).

$$t_{1/2} = \frac{ln(2)}{\lambda}$$

Small assignment

You can try this for yourself! If you know your E. coli bacteria have a growth constant of $\lambda = 0.37$ in the conditions present in your laboratory, you can try to calculate the time it takes for your population to double in size.[4]

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[3] Institute, O. M., Food, A. N. B., & Committee, O. M. N. R. (2002). *Caffeine for the sustainment of mental task performance: Formulations for military operations*. National Academies Press.

[4] The solution is $t = ln(2) \cdot \frac{1}{0.37} \approx 1.87h$

Validating results and determining constants

We will finalise this section on differential equations with a short discussion on the verification of our solution to a DE problem. The easiest way to ensure you have found a correct solution is by checking whether this solution satisfies the DE in question. Going back to an old example, we found a solution

$$y = Ce^{\frac{1}{3}x^3-2x} + 4$$

for the equation

$$\frac{dy}{dx} = (x^2 - 2)(y - 4)$$

and verified this by taking the derivative of our solution

$$\frac{dy}{dx} = \frac{d}{dx}Ce^{\frac{1}{3}x^3-2x} + 4 = (x^2 - 2)Ce^{\frac{1}{3}x^3-2x} = (x^2 - 2)(y - 4)$$

In general, it is good practice to always check your solution in this manner.

However, to stress the usefulness of this verification method, we will now look at an example where we can actually use this to our advantage in solving a rather complex differential equation. Let's consider

$$\frac{d^2y}{dx^2} = 9y$$

Here we encounter something we have not yet discussed: A *second order differential equation*, named after the second order derivative on the left-hand side of this equality, $\frac{d^2y}{dx^2}$. In general, higher order differential equations tend to be harder to solve than lower order DEs. Nonetheless, we can use some educated guesses to find a precise solution to this equation.

As you might have noticed, the general form of this equation

$$\frac{d^2y}{dx^2} = \delta y$$

resembles the differential equation for exponential growth

$$\frac{dy}{dx} = \alpha y$$

From this, we can make the assumption that their solutions might take a similar form. We know that the solution for the exponential growth DE is as follows:

$$y = Ce^{\alpha x}$$

To verify this assumption and further specify the parameter α, let us take the second order derivate of the assumed solution for y

$$\frac{dy^2}{dx^2} = \alpha^2 Ce^{\alpha x}$$

and use this to get a specific solution for our problem:

$$\frac{d^2y}{dx^2} = 9y \rightarrow \alpha^2 Ce^{\alpha x} = 9Ce^{\alpha x}$$

From which we deduce

$$\alpha^2 = 9 \rightarrow \alpha = \pm 3$$

As you can see, we were able to find a correct solution to the given DE by first guessing the form of the answer and then using this guess to determine unknown constants. This is a useful method for solving some differential equations and you will encounter this further during your studies. For now, however, it suffices to realise that this is a valid method of finding a solution and can be a useful way to verify your answer.

Exercises

1. Differential Equations with y-independent right-hand side
    a. $\frac{dy}{dx} = x^3$
    b. $\frac{dy}{dx} = 3e^{2x}$
    c. $\frac{dy}{dx} = \frac{1}{12x}$
    d. $\frac{dy}{dx} = 3x^2 + 5$ with $y(0) = 5$
    e. $\frac{dy}{dx} = \frac{1}{x^2} + 2x$ with $y(1) = 2$
2. Separable Differential equations
    a. $\frac{dy}{dx} = -16yx$
    b. $\frac{dy}{dx} = 6x^2y + xy$ with $y(0) = 8$
    c. $\frac{dy}{dx} = (3x^2 - 5)(y + 3)$ with $y(0) = 6$
    d. $\frac{dy}{dx} = \frac{x+2}{2y}$
3. Exponential Growth/Decay
    a. Give the exponential growth function for a molecule which decays at a rate of $\frac{dN}{dt} = -6N$ (t in hours, N in $mmol$)
    b. Give the timeframe it takes for $\frac{1}{3}$ of the molecules present in 3a to decay.
    c. Imagine a drug that follows exponential decay. 12 hours after the peak blood concentration is at 40%. What is the decay constant λ of this drug?
4. Validating results and determining constants
    a. Verify your solutions to exercises 1 and 2 by taking the first derivatives.
    b. $\frac{d^2y}{dx^2} = 25y$
    c. $\frac{d^2y}{dx^2} = 5\frac{dy}{dx}$
    d. $\frac{dy}{dx} = 5x + 3$ assuming y is of the form $y = ax^2 + bx + c$

II. Chemistry: Reaction Kinetics

Enzymes and the Michaelis-Menten Equation

Life is sustained by the continued action of millions of chemical reactions in living organisms. For example, carbohydrates you ingest has to be broken down and transformed into glucose, before the glucose can be used in the metabolic pathway called *glycolysis* which, as a by-product, provides the molecules ATP and NADH. These two are often described as the energy currency of our bodies and are vital for most other bodily reactions which keep you alive.

In the body, chemical reactions usually have a half-life of less than 1s. This rapid rate of conversion from one molecule into another is only possible with the use of *enzymes*. Enzymes are a class of molecules known as catalysators, which speed up a reaction without being consumed in the reactions – this means that the enzyme is left unchanged and can continue on to react again. Without enzymes, some reactions would have a half-life of up to 2.3 billion years[5] (!) or possibly longer - as you can probably imagine, life as we know it would not be possible if it were based on such slow reactions.

The rate of reactions can be altered which sometimes plays a role in, for example, disease, drug, or genetic manipulation. Therefore, as a Nanobiologist, it is important to know more about these processes.

Enzymatic reaction equation

Enzymatic reactions usually proceed as follows:

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ES} \overset{k_2}{\rightarrow} E + \mathrm{P}$$

The enzyme E and substrate S combine into an intermediary enzyme-substrate complex ES, also known as the *transition state* of the reaction. This complex rapidly dissociates either back into its constituents E and S, or into the enzyme and the product P. In general, first step of an enzymatic reaction tends to be a lot faster than the product-producing step, and so we can assume that the reaction $E + S \rightleftarrows ES$ is in steady state – that is, the same amount of ES dissociates as is produced at any moment in time, and thus the reaction rate $\frac{dES}{dt} = 0$.

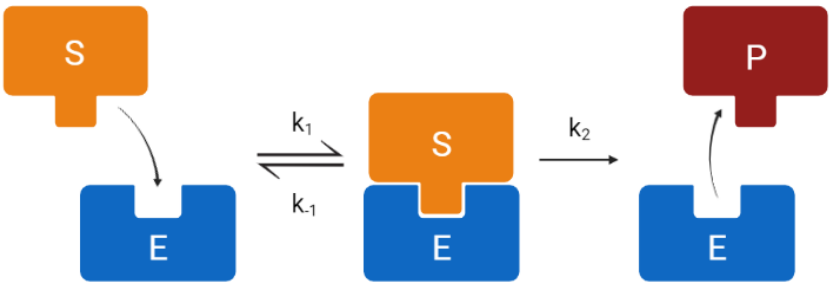

Figure 1
Graphical representation of an enzyme-substrate reaction. The substrate (orange) binds to the enzyme (blue) via a reversible reaction to form the enzyme-substrate complex. A unidirectional reaction then occurs to form the product (red).

[5] *R. R. Wolfenden. (2001). The depth of chemical time and the power of enzymes as catalysts. Accounts of Chemical Research 34(12):938-945. https://doi-org.tudelft.idm.oclc.org/10.1021/ar000058i*

This simple reaction model which holds for most enzymatic reactions allows us to find a universally applicable description for the reaction velocity $\frac{dP}{dt} = V_0$ of such processes, called the *Michaelis-Menten equation.*

Michaelis Menten Equation

The Michaelis-Menten equation can be derived from above enzymatic reaction model and is written as follows:

$$V_0 = \frac{k_2[E]_T[S]}{K_M + [S]}$$

with V_0 the reaction velocity, k_2 the rate constant for the reaction ($[ES] \longrightarrow [E] + [P]$), $[E]_T$ the total enzyme concentration ($[E]_T = [E] + [ES]$), $[S]$ the substrate concentration and finally K_M, the Michaelis constant.

Unfortunately, the derivation of this equation is a bit too lengthy and will not be necessary knowledge for the exam, but feel free to look up online resources if you feel like this will aid your understanding of the equation. Instead, we will focus on the interpretation and use of the MM-equation.

Graphical representation of the Michaelis-Menten equation

Let us now consider what the Michaelis-Menten equation actually represents. On the left-hand side, we have the rate of product formation, or the reaction velocity V_0. On the right-hand side, we can see that this velocity depends on the (total) concentration of the enzyme and the substrate, as well as the rate constant k_2 and the Michaelis-constant K_M. Generally, for a certain enzymatic reaction $k_2$and K_M are fixed quantities and do not vary during the reaction. Similarly, as no enzyme is actually used up in the reaction process, $[E]_T$ is constant as well. Hence this means that usually V_0 will be analysed as a function of $[S]$, which is indeed a quantity which varies during the reaction as substrate gets used up and thus decreases as the reaction proceeds.

Plotting V_0 against $[S]$, we then get our characteristic curve for the MM-equation:

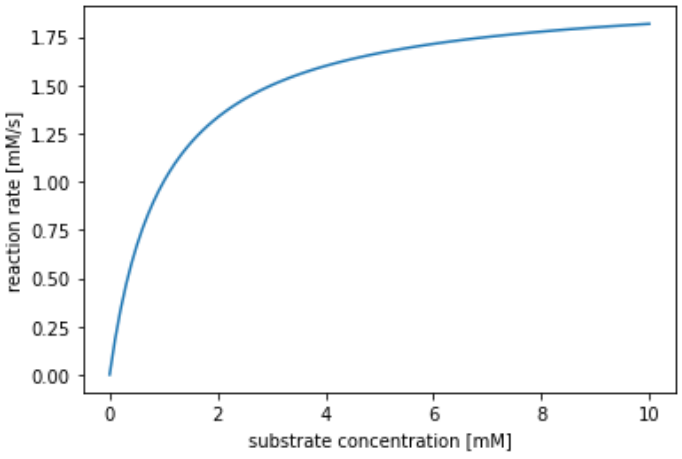

Figure 2: Graph of the Michaelis Menten curve. On the x axis is the substrate concentration in mM and on the y axis there is the reaction rate in mM/2.

As you can see, as the concentration increases, reaction rate V_0 approaches a constant value, in this case $2\frac{mmol}{s}$. This value is the *maximal reaction velocity* V_{max} and is equal to $k_2[E]_T$.

$$V_{max} = k_2[E]_T$$

Small assignment:

Show that V_{max} *is equal to* $k_2[E]_T$ *by taking the limit* $V_{max} = \lim_{[S]\to\infty} \frac{k_2[E]_T[S]}{K_M+[S]}$.

This now allows for a different notation of the MM-equation:

$$V_0 = \frac{V_{max}[S]}{K_M + [S]}$$

We can continue by asking at which point $V_0 = \frac{V_{max}}{2}$. Inserting $V_0 = \frac{V_{max}}{2}$ into the MM equation, we will find a relation between K_M and $[S]$ which has to hold when we reach half the maximal reaction velocity.

Small assignment:

Try finding this relation between K_M *and* $[S]$ *for yourself by doing the required rearrangements.*

You will find that in this case, $K_M = [S]$. Indeed, inserting this into the MM-equation

$$V_0 = \frac{V_{max}[S]}{K_M + [S]} = \frac{V_{max}[S]}{2[S]} = \frac{V_{max}}{2}$$

which verifies our result.

This relation, $K_M = [S]$ when $V_0 = \frac{V_{max}}{2}$ is a vital property of the Michaelis-constant: K_M represents the value of the substrate concentration at which we reach half the maximal reaction velocity. We can thus graphically find the K_M by drawing a horizontal line for $V_0 = \frac{V_{max}}{2}$ and reading of the concentration for this point (this is shown in figure 3). The value of K_M can thus function as an important measure for the reaction dynamics. The smaller K_M, the steeper the MM-curve, the more rapid the rate of production increases. If you take a look at the derivation, you will also find that the K_M gives a specific relationship between the rate constants of

$$\mathrm{E} + \mathrm{S} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ES} \overset{k_2}{\rightarrow} E + \mathrm{P}$$

We define

$$K_M \equiv \frac{k_{-1} + k_2}{k_1}$$

where as before k_2 is the rate constant of the forward reaction ($[ES] \rightarrow [E] + [P]$), and similarly k_1 and k_{-1} are the forward and backward rate constants of $[E] + [S] \rightarrow [ES]$ respectively.

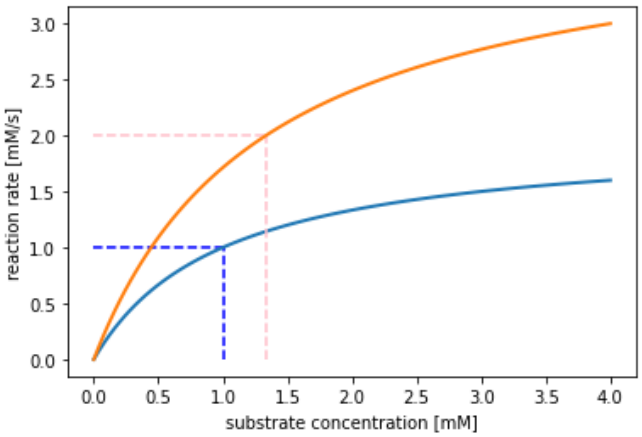

Figure 3
Michaelis-Menten reaction kinetics plot for two different reactions with $V_{max} = 4$ (orange) and $V_{max} = 2$ (blue) respectively. The K_M concentration and reaction velocity $V_0 = V_{max}/2$ are marked for both graphs using dashed lines in pink and dark blue.

Variations on the Michaelis-Menten Equation

Reaction efficiency

When we look at the MM-plot again, we see that the change in reaction velocity is lower the more we increase the concentration of the substrate. What could be the reason for this? The answer is enzyme saturation: When the substrate concentration is low, there are a lot of free enzymes around to take care of all the substrate molecules. Thus, the substrate and enzyme are very likely to bump into each other and bind, starting the conversion (fig 4). In this case, the more substrate there is, the more it can be turned into product in a given timeframe – hence the conversion speed is determined and limited by the amount of substrate present.

However, as the substrate concentration increases, the number of free enzymes (enzymes which are not yet bound to a substrate) decreases, and the chance for a substrate to bump into and bind with an enzyme becomes lower. In this case, the number of enzymes limits the reaction velocity instead of the amount of substrate. Therefore, adding more substrate will not significantly increase the reaction velocity. Both situations are visualized in figure 4.

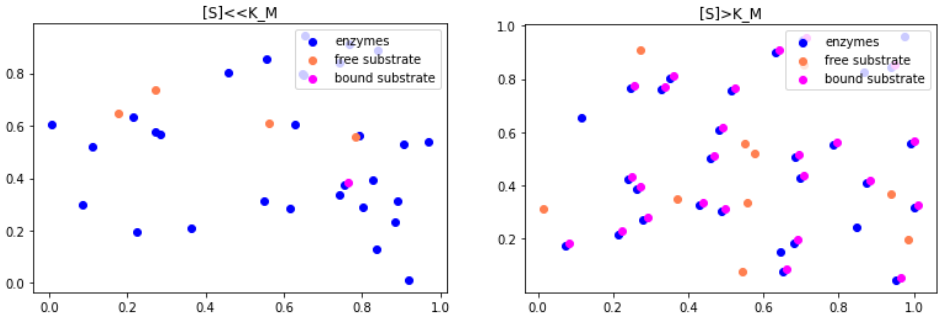

Figure 4
Visual representation of the enzymes and substrate in a reaction. When $[S] \ll K\_M$, the chance for a free substrate and free enzyme to meet is large, and thus adding more substrate increases reaction velocity. Conversely, when the number of free enzymes is low, this chance of a free substrate and enzyme meeting is also low. Thus, increasing the substrate concentration only marginally increases reaction velocity. This is called enzyme saturation.

Now let us take a closer look at the reaction when $S \ll K_M$. This corresponds to the left-hand side of the graph, where the slope of V_0 is relatively high. Mathematically, we can write

$$V_0 = \frac{k_2[E]_T[S]}{K_M + [S]} \approx V_0 = \frac{k_2[E]_T[S]}{K_M}$$

We can see that for constant substrate and enzyme concentrations, V_0 is determined by the coefficient $\frac{k_2}{K_M}$. The value of this coefficient is a measure for the *efficiency* of this enzyme-substrate reaction. We call an enzyme efficient if it is able to convert a substantial proportion of substrate into product. The higher $\frac{k_2}{K_M}$, the more efficient an enzyme is – the higher the proportion of substrate converted.

When is catalytic efficiency high? To answer this question, we must look at when $\frac{k_2}{K_M}$ will be highest. We write

$$\frac{k_2}{K_M} = \frac{k_1 k_2}{k_{-1} + k_2}$$

using the definition of K_M. Now assume the reaction $ES \xrightarrow{k_2} E + P$ to be much faster than the reverse of the enzyme-substrate forming reaction, $ES \xrightarrow{k_{-1}} E + S$, which is generally the case in enzymatic reactions. This will mean that $k_2 \gg k_{-1}$. We can use this to rewrite

$$\frac{k_2}{K_M} = \frac{k_1 k_2}{k_{-1} + k_2} \approx \frac{k_1 k_2}{k_2} = k_1$$

Hence, in this case the reaction velocity is entirely dominated by the reaction rate of the enzyme-substrate complex formation, $E + S \xrightarrow{k_1} ES$. Since the formation rate of ES is dependent on the concentrations of E and S respectively ($\frac{d[ES]}{dt} = k_1[S][E]$), it follows that the idea of a higher substrate concentration leading to a faster reaction velocity indeed holds, assuming our initial conditions still hold as well.

Enzyme Inhibition – Competitive

Unfortunately, the Michaelis-Menten equation is not a complete description of every enzymatic process in nature. An example of this would be the case when substrate is not the only molecule that can bind the active site of the enzyme. A compound which can bind the enzyme and prevent it from reacting with the substrate is called an *inhibitor*. These come in two types: inhibitors who bind the enzyme at the same site as the substrate are termed *competitive*; if an inhibitor binds the enzyme at a different site as the substrate, it is *uncompetitive*. There is actually another type of inhibition called *non-competitive,* but this will not be of interest to us in this reader. Depending on the presence and type of inhibitor, the corresponding MM-Equation has to be adjusted.

Let's first consider the event of a competitive inhibitor being added to our substrate and enzyme mixture (figure 5).

Then the enzyme has two possible reaction pathways:

1. $E + I \underset{k_{-I}}{\overset{k_I}{\rightleftharpoons}} EI$
2. $E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \overset{k_2}{\longrightarrow} E + P$

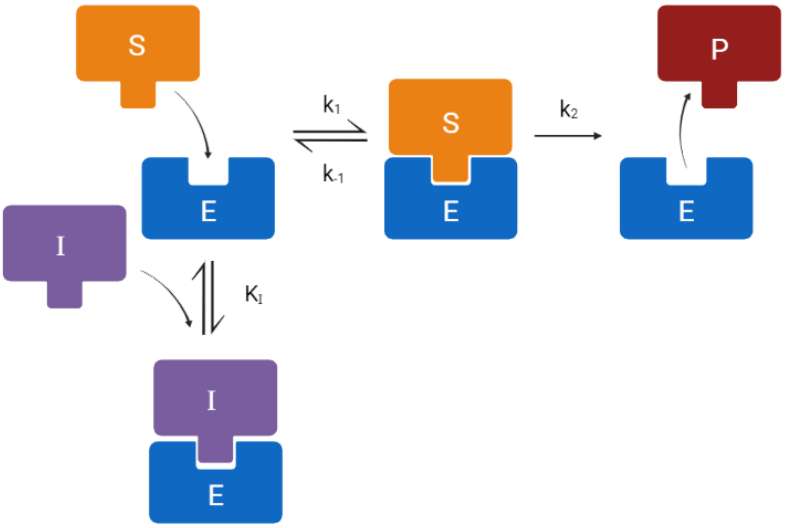

Figure 5
Graphic representation of competitive inhibition. The substrate (orange) and inhibitor (purple) compete for the active site of the enzyme (blue) to either form an enzyme-inhibitor or an enzyme substrate complex. The latter then dissociates into enzyme and product (red).

The second equation we already know, as it corresponds to the product formation equation we have discussed above. The first equation is new, and it describes the formation of an enzyme-inhibitor complex by the enzyme and inhibitor binding.

The effect this has on product formation is that there will be less enzyme available to bind the substrate. This lowered enzyme concentration depends on the rate constant K_I of the enzyme-inhibitor reaction and the inhibitor concentration $[I]$, and is represented by the constant α in a modified Michaelis-Menten equation:

$$V_0 = \frac{V_{max}[S]}{\alpha K_M + [S]}$$

Where $\alpha = 1 + \frac{[I]}{K_I}$ and $K_I = \frac{[E][I]}{[EI]}$.

Now let us visualize what the effect of competitive inhibition on the reaction velocity:

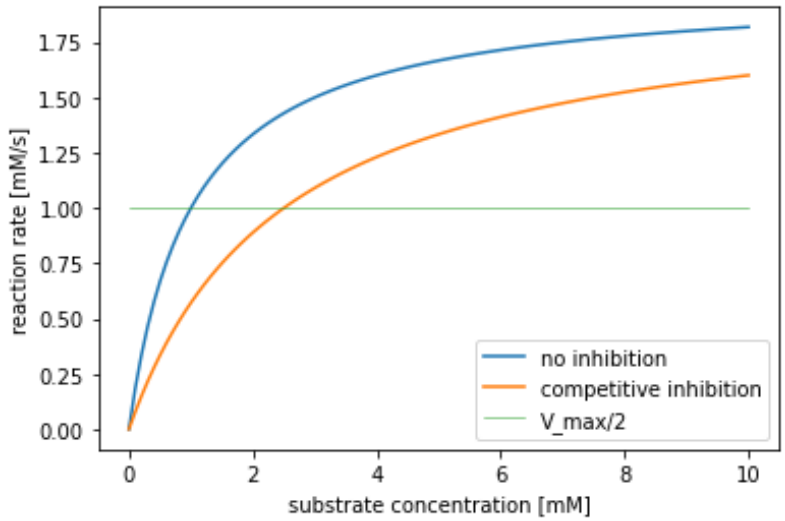

Figure 6
Graph of the Michaelis-Menten Equation for competitive inhibition (orange) and no inhibition (blue). The reaction rate of $V_0 = \frac{V_{max}}{2}$ *is marked in green.*

As we can see, competitive inhibition greatly slows the reaction rate for lower substrate concentrations. The K_M concentration, or the value of $[S]$ for which $\mathrm{V_0} = \frac{\mathrm{V_{max}}}{2}$, of the inhibited reaction thus becomes higher than that of the uninhibited one. In this case, the uninhibited K_M is $[S] = 1$, while the new $K_{MI} = \alpha K_M = 2.5$. However, it is important to note that for competitive inhibition, the V_{max} does not change and for high enough substrate concentrations both the inhibited and the uninhibited reactions proceed at equal speed.

A very common form of competitive inhibition is *product inhibition*. This occurs when the product of a reaction functions as the inhibitor for that reaction. An example of this is the cholesterol pathway in humans: the presence of cholesterol in the blood binds to the enzyme promoting cholesterol formation in the liver, which reduces the number of enzymes available for producing new cholesterol. Thus, this mechanism is part of a negative feedback loop, where the more cholesterol is present, the less it is being produced.These kind of regulation loops are often used in biology, and you will learn much more about them during your studies.

Enzyme inhibition – Uncompetitive

Another type of inhibition is when the inhibitor does not bind the enzyme at the same site as the substrate. This kind of inhibition is most commonly due to inhibitors binding the enzyme-substrate complex before the product is formed. Such binding events then prevent product formation in itself until the complex dissociates.

In equations

1. $E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_{-I'}}{\overset{k_{I'}}{\rightleftharpoons}} ESI$
2. $E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \overset{k_2}{\longrightarrow} E + P$

where the first case results in inhibition.

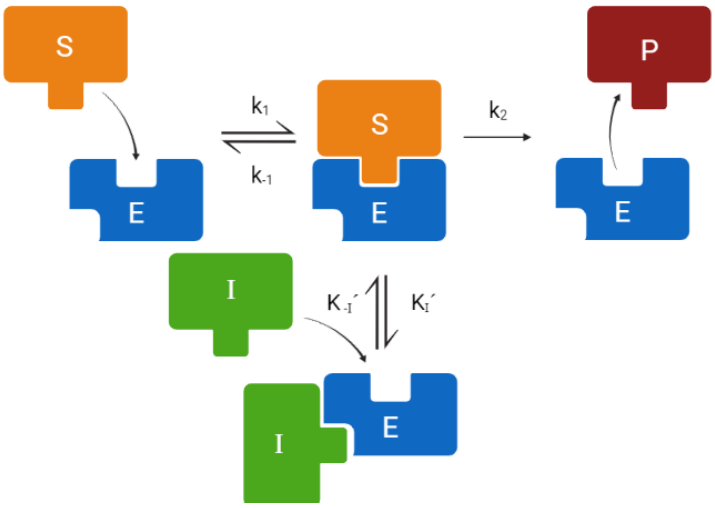

Figure 7
Schematic of uncompetitive enzyme inhibition. Substrate (orange) binds to enzyme (blue) to create the enzyme-substrate complex, which can be either bound by an inhibitor molecule (green) or dissociate into enzyme and product (red).

For uncompetitive inhibition, we write the inhibition rate constant K_I' to distinguish it from competitive inhibition. Again, we can accommodate for this in our Michaelis-Menten Equation by adding constant α' to one of our terms:

$$V_0 = \frac{V_{max}[S]}{K_M + \alpha'[S]}$$

With $\alpha' = 1 + \frac{[I]}{K_I'}$ and $K_I' = \frac{[ES][I]}{[ESI]}$.

The modified Michaelis-Menten graph is shown in figure 8.

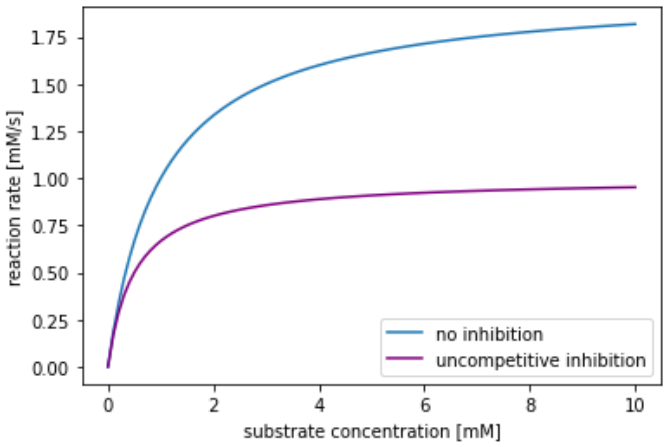

Figure 8
Michaelis-Menten kinetics plotted for uncompetitive (purple) and no inhibition (blue).

The big difference we can observe to both the uninhibited as well as the competitive inhibition cases is that the effective V_{max} and K_M both decrease. The change in V_{max} is due to uncompetitive inhibition decreasing the effective amount of substrate that can be turned into product, as some of it will be bound by the inactivated enzymes.

Combining all possible reaction profiles into one plot we get figure 9:

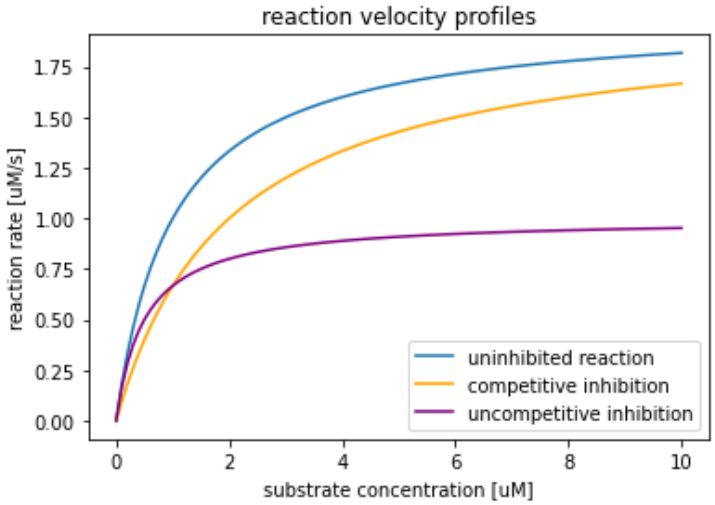

Figure 9
Plotting the reaction velocity profiles for the uninhibited reaction, competitive inhibition ($\alpha = 2$) and uncompetitive inhibition ($\alpha' = 2$)

Exercises

1. What is the catalytic efficiency if $\frac{k_2}{k_2+k_{-1}} \sim 1$?
2. Which parameter(s) are most affected by competitive and uncompetitive inhibition respectively? Explain in 30 words and/or make a sketch.
3. For the uninhibited MM-Equation, how does the reaction velocity change when we increase the following parameter and keep all others constant?
    a. K_m
    b. $[E]_t$
    c. k_2
4. Do we have competitive inhibition if $[I] = K_I$ and $[S] \gg 2K_M$?
5. Calculate the K_M for an enzyme with $V_0 = 6\mu M s^{-1}$, $Vmax = 10\mu M s^{-1}$ and $[S] = 300\mu M$
6. Can uncompetitive inhibition be overcome by adding more substrate?
7. Calculate the total substrate concentration you need for a reaction at 85% of the maximal reaction velocity for $K_M = 20\mu M$
8. Calculate the total substrate concentration you need for a reaction at 85% of the maximal reaction velocity for $K_M = 20\mu M$ and competitive inhibition with $[I] = 0.1\mu M$ and $K_I = 0.4\mu M$

III. Physics: Diffusion

The existence of atoms

Humanity has always wondered about the fundamental elements of nature and how they behave. There have been many philosophers around the globe who imagined the universe to consist of tiny, indivisible particles, 'atoms' as the ancient Greeks called them, the smallest elements of matter. However, in the 19th century this viewpoint was not very popular in the West. In the early 1800's, the botanist Robert Brown observed under a microscope that tiny pollen particles in solution showed a very irregular, jittery motion. First thinking that it could be the 'vis viva', the 'life force', he repeated the experiments with lifeless dust particles and observed the same type of motion. Almost a century later, this type of motion contributed to a revolution in science. Jean Perrin measured the movement of small solutes and discovered that it was well described by an equation from a paper by a young Albert Einstein. Twenty years later, Perrin was awarded the Nobel Prize for his contributions to "the discontinuous structure of matter". His experiment and others suddenly revealed that the atomistic world view is actually very useful, and nowadays it seems impossible to detach from it.

The diffusion equation

The irregular motion of molecules in solution is well described by the 'random walk' (a mathematical description that we will skip for now), and the spreading of molecules in solution obeys the diffusion equation. This equation does not only describe the spreading of molecules, but also the spreading of heat, the shape of flexible polymers, genetic drift, the average motion of motile bacteria, and, among many other applications, even certain aspects of financial markets. In one dimension, it reads

$$\frac{\partial \rho}{\partial t} = D \frac{\partial^2 \rho}{\partial x^2}$$

with $\rho(x,t)$ (the Greek letter 'rho') indicating the concentration of a solute at position x and time t, and D the diffusion constant. One can see from the equation that the dimension of D is area per time. If one would release a solute at $x = 0$ at $t = 0$ (for example by injecting it there at $t = 0$) the solute will spread out over time, according to the diffusion equation. Under those conditions, the solution of the equation is:

$$\rho(x,t) = \frac{N}{\sqrt{4\pi D t}} e^{-\frac{x^2}{4Dt}}$$

with N the total number of particles.

Figure 10 shows the solution for several values of t and $D = 1 \cdot 10^{-9}\ \mathrm{m}^2/\mathrm{s}$.

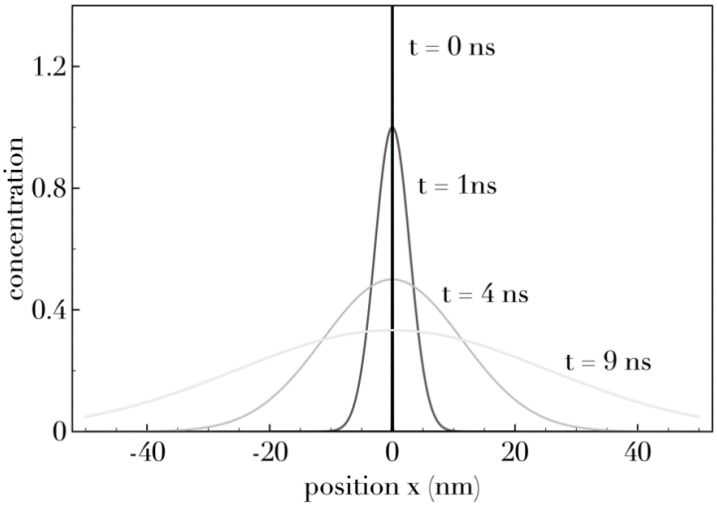

Figure 10 The concentration of a solute as a function of position, at different times

For small particles in a fluid, the Stokes-Einstein equation relates the diffusion constant to the viscosity of the fluid

$$D = \frac{k_B T}{6\pi\eta r}$$

* (Actually, this equation is only valid if the "Reynolds number" is small, but you can believe for now that this is certainly the case for microscopic particles in water).

In the equation k_B is the Boltzmann constant, T the temperature in Kelvin, η the viscosity of the fluid, and r the radius of the particles. For simple ions in water, the diffusion constant is of the order of $10^{-9}\ \mathrm{m}^2/\mathrm{s}$.

Drag on a particle

The Stokes-Einstein constant can also give us information about the drag a particle experiences as it moves around in its environment. Generally, the drag force F_d acting on an object swimming, or drifting around in a medium can be described as

$$F_d = -\gamma v$$

Where

$$\gamma = 6\pi\eta R$$

And the minus sign indicates that the force is opposite to the motion of the particle, v is the velocity of the particle and γ is known as the drag coefficient, a constant which relates the two previously described parameters. This drag coefficient is related to the Diffusion coefficient D via the Einstein relation:

$$\gamma D = k_B T$$

Thus, experimental measurements of the drag on a particle gives us an information about its diffusion coefficient.

Average position and variance of a diffusing particle

The diffusion equation can also be used to describe the probability of finding a diffusing particle in a neighborhood of position x at time t. If the particle is released at $x = 0$ at $t = 0$, this probability density function is

$$P(x,t) = \frac{1}{\sqrt{4\pi D t}} e^{-\frac{x^2}{4Dt}}$$

The mean of the position at time t is then

$$\langle x \rangle = \int_{-\infty}^{\infty} x P(x,t) dx$$

and without doing any math, one can conclude that it should be zero at all times. The function P is even (symmetric around $x = 0$), and x is odd (antisymmetric around $x = 0$), so the integral should be zero. Another way of reasoning is that the average should be zero, because the particle has no preference of direction. It diffuses to the left and to the right with equal probability.

However, the variance of the probability density function is

$$\langle x^2 \rangle = \int_{-\infty}^{\infty} x^2 P(x,t) dx = 2Dt$$

The variance is a good measure for the 'width' of the curves $d = \sqrt{\langle x^2 \rangle} = \sqrt{2Dt}$, which represents the part of space that a diffusing particle typically explores in a time t. Here we find a very peculiar law between the distance d and time t, that

$$d \sim \sqrt{t}$$

(d is proportional to the square root of t)

Thus, if it takes 1 ns to explore 5 nm, it would take 100 ns to explore 50 nm, about 1ms to explore 5 μm, and... about a day for 5 cm! Just to illustrate this scaling law, see how much effort it takes for a diffusing particle to explore space in the following table:

d	t
5 nm	1 ns
5 μm	1 ms
5 mm	1000 s
5 m	32 years

Short distances are explored quickly, but it becomes increasingly more difficult to explore larger distances. Large organisms clearly cannot rely on diffusion alone to transport substances throughout the body, and even single cells make use of molecular motors and ion pumps to speed up the exchange and organisation of components. The same conclusion can be drawn about the spreading of heat, or the spreading of droplets in the air, or the exploration of motile bacteria. Without other principles like convection (air currents) or directed motion, this process does not get very far.

However, as diffusion is very efficient when it comes to motion on small scales, it is an essential process for a multitude of biological systems. Many hormones and salts use diffusion to cross short distances, and in your lungs, oxygen diffuses from the alveoli into the bloodstream, where it is picked up by red blood cells to be distributed throughout your body. Conversely, insects do not have a way to actively carry oxygen through their body and rely solely on oxygen diffusion trough tubes in their body. Throughout prehistory, researchers have observed a correlation between oxygen concentration in the air and insect size – since oxygen supply to the insects' inner body is limited by diffusion, lower oxygen concentration in the air cannot sustain large sizes. Thus, very high oxygen concentration in the air was one of the major reasons why insects in the Carboniferous and early Permian eras could grow so big! This is a prime example of how nanoscale phenomena can greatly influence life on earth.

Exercises

All these processes are assumed to take place at 300K (about room temperature). You may use that the viscosity of water η = 1mPas and $k_BT = 4.14 \cdot 10^{-21}$J.

1. Assume a bacterium with $D = 5 \cdot 10^{-12} m^2 s^{-1}$.
   a. What is the radius of the bacterium?
   b. Give the value of the drag force it experiences while swimming at $25 \mu m s^{-1}$?
2. Give a bacterium of $r = 500nm$, which is accelerating at $100 nm s^{-2}$. How strong of a drag force does it experience after 10s, starting with v(0) = 0? Assume there is no drag: how far does it travel in 10s, if initial velocity is $15 \mu m s^{-1}$?
3. Consider a molecule which has a diameter of $2\mu m$. How far does it get in 100 years?
4. Investigate: Which factors increase the distance travelled by diffusion when increased? Which decrease this distance?

Solutions to the exercises

Solutions to part I Mathematics: Differential Equations

1. Differential equations with y-independent right-hand side

a. $y = \frac{1}{4}x^4 + C$

$$\frac{dy}{dx} = x^3 \longrightarrow dy = x^3 dx \longrightarrow \int dy = \int x^3\, dx \longrightarrow y = \frac{1}{4}x^4 + C$$

b. $y = \frac{3}{2}e^{2x} + C$

$$\frac{dy}{dx} = 3e^{2x} \longrightarrow dy = 3e^{2x} dx \longrightarrow \int dy = \int 3e^{2x}\, dx \longrightarrow y = \frac{3}{2}e^{2x} + C$$

c. $y = \frac{1}{12}ln(x) + C$

$$\frac{dy}{dx} = \frac{1}{12x} \longrightarrow dy = \frac{1}{12x}dx \longrightarrow \int dy = \int \frac{1}{12x}dx \longrightarrow y = \frac{1}{12}ln(x) + C$$

d. $y = x^3 + 5x + 5$

$$\frac{dy}{dx} = 3x^2 + 5 \longrightarrow dy = (3x^2 + 5)dx \longrightarrow \int dy = \int (3x^2 + 5)dx \longrightarrow y$$
$$= x^3 + 5x + C$$
$$y(0) = 5 = 0^3 + 5 \cdot 0 + C = C \longrightarrow C = 5$$

e. $y = -\frac{1}{x} + x^2 + 2$

$$\frac{dy}{dx} = \frac{1}{x^2} + 2x \longrightarrow dy = \left(\frac{1}{x^2} + 2x\right)dx \longrightarrow \int dy = \int \left(\frac{1}{x^2} + 2x\right)dx \longrightarrow \int dy$$
$$= \int \frac{1}{x^2}dx + \int 2xdx \longrightarrow y = -\frac{1}{x} + x^2 + C$$
$$y(1) = -1 + 1^2 + C = 2 \longrightarrow C = 2$$

2. Separable Differential equations

a. $y = Ce^{-8x^2}$

$$\frac{dy}{dx} = -16yx \longrightarrow \frac{dy}{y} = -16xdx \longrightarrow \int \frac{dy}{y} = \int -16x\, dx \longrightarrow ln(y) = -8x^2 + C$$
$$\longrightarrow y = Ce^{-8x^2}$$

Note that just as in the reader text, we combined the constants of both sides of the equation into a common constant $C = C_2 - C_1$

b. $y = 8e^{2x^3 + \frac{1}{2}x^2}$

$$\frac{dy}{dx} = 6x^2y + xy \longrightarrow \frac{dy}{dx} = (6x^2 + x)y \longrightarrow \frac{dy}{y} = (6x^2 + x)dx \longrightarrow \int \frac{dy}{y}$$
$$= \int (6x^2 + x)dx \longrightarrow ln(y) = 2x^3 + \frac{1}{2}x^2 + C \longrightarrow y = Ce^{2x^3 + \frac{1}{2}x^2}$$
$$y(0) = Ce^{2 \cdot 0^3 + \frac{1}{2} \cdot 0^2} = 8 \longrightarrow C = 8$$

c. $y = 9e^{x^3 - 5x} - 3$

$$\frac{dy}{dx} = (3x^2 - 5)(y + 3) \longrightarrow \frac{dy}{y + 3} = (3x^2 - 5)dx \longrightarrow \int \frac{dy}{y + 3} = \int (3x^2 - 5)dx$$
$$\longrightarrow ln(|y + 3|) = x^3 - 5x + C \longrightarrow y + 3 = Ce^{x^3 - 5x} \longrightarrow y$$
$$= Ce^{x^3 - 5x} - 3$$
$$y(0) = Ce^{0^3 - 5 \cdot 0} - 3 = 6 \longrightarrow C - 3 = 6 \longrightarrow C = 9$$

d. $y = \pm\sqrt{\frac{1}{2}x^2 + 2x + C}$

$$\frac{dy}{dx} = \frac{x+2}{2y} \longrightarrow 2ydy = (x+2)dx \longrightarrow \int 2y\,dy = \int (x+2)dx \longrightarrow y^2$$
$$= \frac{1}{2}x^2 + 2x + C \longrightarrow y = \pm\sqrt{\frac{1}{2}x^2 + 2x + C}$$

3. Exponential Growth/Decay
   a. $N(t) = N_0 e^{-6t}$
   $$\frac{dN}{dt} = -6N \longrightarrow \frac{dN}{N} = -6dt \longrightarrow \int \frac{dN}{N} = \int -6\,dt \longrightarrow ln(N) = -6t + N_0 \longrightarrow N(t) = N_0 e^{-6t}$$
   b. $t \approx 0.0676(h)$
   $$N(t) = \frac{2}{3}N_0 = N_{0e^{-6t}} \longrightarrow \frac{2}{3} = e^{-6t} \longrightarrow ln\left(\frac{2}{3}\right) = -6t \longrightarrow t = -\frac{ln\left(\frac{2}{3}\right)}{6} \approx 0.0676(h)$$
   c. $\lambda \approx 0.0764(h^{-1})$
   $$N(12) = 0.4N_0 = N_0 \mathrm{e}^{-12\lambda} \longrightarrow ln(0.4) = -12\lambda \longrightarrow \lambda = -\frac{\ln(0.4)}{12} \approx 0.0764(\mathrm{h}^{-1})$$
4. Validating results and determining constants
   a. See whether the derivatives correspond to the differential equations given in the exercises.
   b. $y = Ce^{\pm 5x}$
   We assume the solution has the form $y = Ce^{\alpha x}$ (explanation in text)
   $$y = Ce^{\alpha x} \longrightarrow \frac{d^2y}{dx^2} = C\alpha^2 e^{\alpha x}$$
   $$\frac{d^2y}{dx^2} = 25y \longrightarrow C\alpha^{2e^{\alpha x}} = 25Ce^{\alpha x} \longrightarrow \alpha^2 = 25 \longrightarrow \alpha = \pm 5 \longrightarrow y = Ce^{\pm 5x}$$
   c. $y = Ce^{5x}$
   We assume the solution has the form $y = Ce^{\alpha x}$ (explanation in text)
   $$y = Ce^{\alpha x} \longrightarrow \frac{\mathrm{dy}}{\mathrm{dx}} = C\alpha \mathrm{e}^{\alpha \mathrm{x}} \longrightarrow \frac{d^2y}{dx^2} = C\alpha^2 e^{\alpha x}$$
   $$\frac{d^2y}{dx^2} = 5\frac{dy}{dx} \longrightarrow C\alpha^2 e^{\alpha x} = 5C\alpha e^{\alpha x} \longrightarrow \alpha = 5 \longrightarrow y = Ce^{5x}$$
   d. $y = \frac{5}{2}x^2 + 3x + C$
   $$y = ax^2 + bx + c \longrightarrow \frac{dy}{dx} = 2ax + b$$
   $$\frac{dy}{dx} = 5x + 3 \longrightarrow 2ax + b = 5x + 3 \longrightarrow a = \frac{5}{2}\ \&\ b = 3 \longrightarrow y = \frac{5}{2}x^2 + 3x + C$$

Solutions to part II Chemistry: Reaction Kinetics

1. Using
$$\frac{k_2}{K_M} = \frac{k_1 k_2}{k_{-1} + k_2}$$
we see that the catalytic efficiency becomes equal to k_1.
2. See the corresponding sections in the reader
3. We use
$$V_0 = \frac{V_{max}[S]}{K_M + [S]}$$
meaning that the value
    a. Decreases
    b. Increases
    c. Increases
4. No. In case of $[I] = K_I$ we have
$$\alpha = 1 + \frac{[I]}{K_I} = 2$$
and thus
$$V_0 = \frac{V_{max}[S]}{2K_M + [S]}$$
Now using $[S] \gg 2K_M$ we get that
$$V_0 \approx \frac{V_{max}[S]}{[S]}$$
which means the effect of the inhibition will not significantly affect the reaction.
5. We can rearrange the Michaelis-Menten equation
$$V_0 = \frac{V_{max}[S]}{K_M + [S]}$$
to
$$K_M = \frac{(V_{max})[S]}{V_0} - [\mathrm{S}]$$
Inserting the given values, we arrive at $K_M = 200\mu M$
6. No. As we can see from the graphical representation, uncompetitive inhibition alters the value of V_{max}. This occurs as some substrate will be bound by the inhibitors instead. If we increase our substrate concentration to be very large, we can increase the V_{max} to be close to that of the uninhibited reaction, but it is impossible to fully overcome the effects of inhibition.
7. We use the Michaelis-Menten equation
$$V_0 = \frac{V_{max}[S]}{K_M + [S]}$$
First, realize that we can write $V_0 = 0.85V_{max}$ which reduces our equation to
$$\frac{V_0}{V_{max}} = 0.85 = \frac{[S]}{K_M + [S]}$$
We can now rearrange this
$$[S] = \frac{0.85K_M}{1 - 0.85}$$
Using our given value for K_M we arrive at the solution $[S] = 113.33\mu M$.
8. This question can be answered very similarly to question 7, except we need to use the equation for competitive inhibition
$$V_0 = \frac{V_{max}[S]}{\alpha K_M + [S]}$$

The difference here is that we have an altered K_M, so rearranged our equation becomes

$$[S] = \frac{0.85\ \alpha\ K_M}{1 - 0.85}$$

We can calculate α by using the relation

$$\alpha = 1 + \frac{[I]}{K_I} = 1.25$$

Now we can find our value for $[S]$ to be $[S] = 141.67\mu M$

Solutions to part III Physics: Diffusion

1. We can rearrange

$$D = \frac{k_B T}{6\pi\eta r} \rightarrow r = \frac{k_B T}{6\pi\eta D}$$

Inserting the given values into the equation, we get $r = 43{,}9nm$. For b, we use

$$\gamma D = k_B T \rightarrow \gamma = \frac{k_B T}{D} = 8.28 \cdot 10^{-10}\,\frac{Js}{m^2}$$

And insert this into

$$F = -\gamma v$$

to obtain $F = -2.07 \cdot 10^{-14} N$.

2. We can obtain the velocity from the acceleration via Newton's laws of motion:

$$v(t) = \int a(t)dt = a(t)t + v(0)$$

where we have given that v(0)=0. We can then calculate

$$v(10) = 100nms^{-2} \cdot 10s = 1\mu ms^{-1}$$

The frictional drag coefficient is given by

$$\gamma = 6\pi\eta r = 9.425 \cdot 10^{-9} Jsm^{-2}$$

Then $F = -\gamma v = -9.425 \cdot 10^{-15} N$.

The distance travelled can again be found using Newton's laws of motion and integrating in time from 0 to 10s.

$$x(10) = \int_0^{10} a(t)t + v(0)dt = \left[\frac{at^2}{2} + v(0)t\right]_0^{10} = \left[\frac{100nms^{-2} \cdot t^2}{2} + 15\mu m \cdot t\right]_0^{10}$$
$$= 155\mu m$$

3. We know that the average distance travelled

$$\langle x^2 \rangle = 2Dt \rightarrow x = \sqrt{(2Dt)}$$

100 years has $60 \cdot 60 \cdot 24 \cdot 365 \cdot 100 = 3.1536 \cdot 10^9 s$ We obtain D via filling in the necessary values in

$$D = \frac{k_B T}{6\pi\eta r} = 2.2 \cdot 10^{-13} m^2 s^{-1}$$

Filling D and t into our first equation, we find the average distance travelled to be about $0.037m = x$.

4. From

$$\langle x^2 \rangle = 2Dt = 2 \cdot \frac{k_B T}{6\pi\eta r} \cdot t$$

We can see that the distance increases with temperature and time but decreases as viscosity and radius increase. *Does this make sense to you? Can you give suggestions to what causes these parameters to influence the distance in such a way?*

Formulas you have to know

$t_{1/2} = \frac{ln(2)}{\lambda}$ Relation between half-life and decay constant

(note: You can also just rederive this relation yourself on the exam with the knowledge in this reader)

$V_0 = \frac{k_2[E]_T[S]}{K_M+[S]}$ Michaelis-Menten equation, no inhibition

$V_0 = \frac{V_{max}[S]}{\alpha K_M+[S]}$ Michaelis-Menten equation, competitive inhibition

$V_0 = \frac{V_{max}[S]}{K_M+\alpha'[S]}$ Michaelis-Menten equation, uncompetitive inhibition

$\gamma = 6\pi\eta r$ Drag coefficient

$F_d = -\gamma v$ Drag force

$\gamma D = k_B T$ Stokes-Einstein relation

$d = \sqrt{\langle x^2 \rangle} = \sqrt{2Dt}$ Mean-Squared-Distance of diffusion processes