

Calculus

Calculus for Bioinformatics

- Providing background in calculus to deal with requirements in other mathematical, computational or modelling issues to appear further.
- Providing calculus tools and strategies to endow the student with a minimal experience to study biological phenomena in a formal and cooperative way.

- Acquire an intra- and interdisciplinary training in both computational and scientific subjects with a solid basic training in biology.
- To acquire knowledge and understanding in a field of study that starts from the basis of general secondary education, and is typically at a level that although it is supported by advanced textbooks, includes some aspects that involve knowledge of the forefront of their field of study.
- To know how to apply the acquired knowledge to the work or vocation in a professional manner and have competencies typically demonstrated through devising and defending arguments and solving problems within their field of study.
- To be able to convey information, ideas, problems and solutions to both specialist and non-specialist audiences.
- Develop the skills needed to undertake further studies with a high degree of autonomy.
- To manage and exploit all kinds of biological and biomedical information to transform it into knowledge.
- To apply mathematical foundations, algorithmic principles and computational theories in the modeling and design of biological systems.
- To identify meaningful and reliable sources of scientific information to substantiate the state of arts of a bioinformatic problem and to address its resolution.

We distinguish 3 types of sessions: theory, seminars and lab.

- **Theory** sessions will be basically devoted to the so-called *conceptual line*.
- **Seminar and Lab** sessions will be basically devoted to the so-called *practical line*. In both type of sessions, the students will develop proposed problems.
- In the **lab** sessions, we will focus mostly on projects requiring the use of computer tools.

Conceptual line: It will consist of introductory lectures, motivated by specific biological problems. The contents of the course will be:

- Interpolation and approximation.

- Continuity and differentiability.

- Integration.

- Differential equations and dynamical systems.

- Numerical methods.

Every subject will include both expository sessions by the teaching staff and problem solving sessions.

Practical line: It will turn around short projects where the previous motivational biological problems will be extended. As the course evolves, the projects will integrate concepts and techniques from different chapters.

Instances of topics for these problems, which will be described using models as simple as possible, are:

- Population dynamics.
- Models in epidemiology.
- Models of neuron activity.

Attention hours will hold after every session by appointment.

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The use of the software **Octave** (or Matlab) will be essential both in Seminar and Lab sessions.

Octave (<https://www.gnu.org/software/octave/>, distributed under the terms of the *GNU General Public License*).

The support material (slides, problem/project lists, scientific papers, . . .) will be posted and updated during the course at the **aula@-ESCI**.

- Ledder, Glenn. *Mathematics for the Life-Sciences: Calculus, Modeling, Probability and Dynamical Systems*, Springer Undergraduate Texts in Mathematics and Technology, New York : Springer, 2013. ISBN: 978-1-461-47276-6.
- Strang, Gilbert. *Calculus*, 2nd edition, Wellesley-Cambridge Press, 2010. ISBN 978-09802327-4-5. Also available at the MIT Open CourseWare.
<http://ocw.mit.edu/resources/res-18-001-calculus-online-textbook-spring-2005/textbook/>
- Allman, Elizabeth S.; Rhodes, John A. *Mathematical models in biology: an introduction*. Cambridge: Cambridge University Press, 2004. ISBN 978-0-521-81980-0. See http://cataleg.upc.edu/record=b1297072 S1*cat
- Istas, Jacques. *Mathematical modeling for the life sciences* [on line]. Berlin: Springer, 2005. Available on: <http://dx.doi.org/10.1007/3-540-27877-X>. ISBN 354025305X.

- Salas, Saturnino L.; Etgen, Garret T.; Hille, Einar. *Calculus: One and Several Variables*, 10th Edition. Wiley [hardcover: January 2007, ISBN : 978-0-471-69804-3] [electronic version: August 2010, ISBN: 978-0-470-47276-7]
- Ermentrout, Bard G.; Terman, David H. *Mathematical foundations of neuroscience*. New York: Springer, 2010. ISBN 978-0-387-87708-2.
- Hirsch, Morris W.; Smale, Stephen. *Differential equations, dynamical systems, and linear algebra*. Academic Press; American Elsevier Publishing Co., 1975. ISBN : 978-0-720-42609-0.
- Murray, J.D. *Mathematical biology* [on line]. 3rd ed. Berlin: Springer, 2002. Available on: <http://link.springer.com/book/10.1007/b98868> (volume 1). ISBN 978-0-387-95223-9.
- Keener, James P.; Sneyd, James. *Mathematical physiology*. Vol 1. 2nd ed. New York: Springer Verlag, 2009. ISBN 978-0-387-75846-6.

- A1 Assessment of the concepts and seminar projects introduced in Weeks 1–4. Week 5 (October 17th). Weight/value: 20%+10%
- A2 Assessment of practical abilities in solving short projects. Week 10 (November 23rd). Weight/value: 20%
- A3 Assessment of concepts and projects introduced along the course. Week 12 (December 12th). Weight/value: 50%

To obtain a PASS it is necessary to have obtained a grade above 3 over 10 in A1, A2 and A3.

Calculus and modeling

Calculus (from Latin *calculus*, literally "small pebble used for counting") is the mathematical study of change, in the same way that geometry is the study of shape and algebra is the study of operations and their application to solving equations.

Calculus has two major branches:

- differential calculus (concerning rates of change and slopes of curves);
- integral calculus (concerning accumulation of quantities and the areas between curves);

Both branches are related to each other by the *fundamental theorem of calculus*.

Modern calculus is considered to have been developed from 17th century by Isaac Newton and Gottfried Leibniz.



Isaac Newton (1643-1727)



Gottfried W. Leibniz (1646-1716)

The Kerala school in India had already developed some rudiments of calculus at least 200 years before!

Calculus is one of the greatest intellectual achievements of humankind. It allows us to solve mathematical problems that cannot be solved with ordinary algebra, and that in turn allows us to make predictions about the behavior of real-world systems that could not be made with algebra alone. (Ledder)

The sciences do not try to explain, they hardly even try to interpret, they mainly make models. By a model is meant a mathematical construct which, with the addition of certain verbal interpretations, describes observed phenomena. The justification of such a mathematical construct is solely and precisely that it is expected to work-that is, correctly to describe phenomena from a reasonably wide area. (Von Neumann)



John von Neumann
(1903-1957)

A mathematical model is a description of a system using mathematical concepts and language.

A mathematical model is an approximation of a real phenomenon, that has to be tested by experiment.

The model has a certain scope, a validity domain.

A model may help to explain a system and to study the effects of different components, and to make predictions about behavior.

Qualitative models: idealized models that let us to describe the main features of a phenomenon.

Quantitative models: let us to make predictions, and simulations.

Mathematical models

An example: the planetary motions (I)

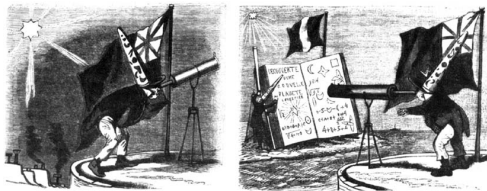
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- Johannes Kepler (1571-1630), mathematician and astronomer, discovered that the Earth and the rest of planets move in elliptic orbits around de Sun, *postulating* the three fundamental laws of the planetary motions.



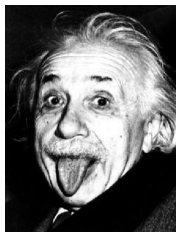
- Isaac Newton (1643-1727), mathematician, physicist and astronomer, *mathematically proved* the three Kepler's laws from his own laws of motion and law of universal gravitation.

- U.J. Le Verrier (1811-1877) and J.C. Adams (1819-1892), independently, *predicted* the existence of an eighth planet perturbing the orbit of Uranus, that was discovered in 1791.
- The planet Neptune was discovered by the astronomer J.G. Galle in 1845, in the previously computed position.



A cartoon published in France about the controversy over the discovery of Neptune. Adams seeks the planet and finds it in the pages of Le Verrier's book.

- Le Verrier discovered in 1859 a *discrepancy* in the orbit of Mercury, that was not predicted by Newton's mechanics.
- Albert Einstein (1879-1955), physicist-mathematician, improved the theory of gravitation in 1915, with the *Theory of General Relativity*, and explained the orbit of Mercury.



Newton's gravitational theory is nowadays used in most of the space missions.

Einstein's gravitational theory is used in the Global Positioning System (GPS).

An evolutionary process, a system that evolves with time, is said to be:

- *finite-dimensional* if the phase space, the set of all possible states of the process, can be identified with an (open) set of the n -dimensional space;
- *deterministic* if its evolution is determined by its state at the present time;
- *differentiable* if the evolution depends not only continuously, but also differentiably, with respect to time, the state at the present time and other parameters of the phenomenon.

The identification of phase space with an n -dimensional space lead to the *geometrization* of evolutionary processes, since evolutions are identified with graphs of functions of the state variables with respect to time, known as *trajectories*.

The properties of continuity and differentiability are very useful to make *predictions*:

- since initial data and parameters are only known with finite accuracy, *continuity* is important to avoid “jumps” in the behavior of the system when slightly perturbing it;
- *differentiability* is useful to estimate rates of changes with respect to time (velocity), initial conditions and parameters;
- predictions are produced by *integrating* the law of evolution of the system, which encodes the relations between the velocities and the states.

Previous properties are *local*, but when one considers *global* properties there is room for:

- changes in the qualitative structure of a given family of evolutionary processes (bifurcation theory);
- long-term unpredictability (chaos theory).

These matters are studied by the theory of dynamical systems.

Pharmacokinetics studies the manner and speed with which drugs and their metabolites are eliminated by the various excretory organs.

A model for the amount $y(t)$ of a drug in a human body at a time t is given the formula

$$y(t) = e^{-\kappa t} A,$$

where A, κ are parameters, which play different roles:

- A is the initial dose (at time 0);
- κ is the elimination rate constant, and it is the parameter of the model.

The state of the system (for a given κ) is described by the amount of the drug, y , and then the phase space is the interval $]0, +\infty[$.

The extended phase space (i.e. including time) is $\mathbb{R} \times]0, +\infty[$.

Example¹. Jan takes two tablets of acetaminophen (paracetamol) for her headache, so that the dose is 650 mg. The elimination rate constant is $\kappa = 0.3 \text{ h}^{-1}$.

Question. At what time will there be only 130 mg of acetaminophen in Jan's system?

Solution. Given $y = 130 \text{ mg}$, we have to find t so that $y = e^{-\kappa t} A$. An easy computation leads to the formula ²

$$t = \frac{1}{\kappa} \log \left(\frac{A}{y} \right).$$

In particular, for the specific problem we are solving, $t = \frac{1}{0.3} \log 5 \simeq 5.36 \text{ h}$.

¹Example 1.1.1 in Ledder's

²In the following log means natural logarithm, the inverse of the exponential function.

The fact that the model depends continuously on parameters let us to rely in the results. Small discrepancies either in parameter or the dose produce just small discrepancies in the results.

The elimination rate constant κ can depend not only on the specific drug, but also on the age, sex, weight and many other instances that depend on the individual. But the results are qualitatively the same.

Question. At what time Jan's system has half of the initial amount of acetaminophen?

Solution. We are asked to find $t_{\frac{1}{2}}$ so that $y(t_{\frac{1}{2}}) = \frac{1}{2}A$. This is very easy from the previous formula:

$$t_{\frac{1}{2}} = \frac{\log 2}{\kappa} \simeq 2.31\text{h}$$

Observations:

- $t_{\frac{1}{2}}$ is the *half-life* for the constant decaying system;
- $t_{\frac{1}{2}}$ depends on κ , and it does not depend on the initial dose;
- Public resources generally provide this quantity for a given drug rather than the elimination rate κ , but

$$\kappa = \frac{1}{t_{\frac{1}{2}}} \log 2.$$

The rate of change of the amount of drug is the derivative with respect to time:

$$\dot{y}(t) = -\kappa e^{-\kappa t} A.$$

The velocity and the state itself are related by

$$\dot{y}(t) = -\kappa y(t).$$

This is the law of the decay of the drug, a *differential equation* that encodes all possible evolutions of the system.

Similar laws describe other *a priori* very different phenomena, such as radioactive decay (useful for ^{14}C dating test) and cooling of bodies.

In general, the differential equation of an evolutionary process is the equation that relates the rates of change of the states with the states themselves.

An evolution of the system is (presumably) determined by the initial condition, say $y(0) = A$.

We have then to solve an *initial value problem*:

$$\dot{y}(t) = -\kappa y(t), \quad y(0) = A.$$

Notice that $y(t) > 0$, so that we can divide by $y(t)$ to get

$$-\kappa = \frac{\dot{y}(t)}{y(t)} = \frac{d}{dt}(\log y(t)).$$

Integrating from time 0 to t both sides of the equation, we get:

$$-\kappa t = \int_0^t \frac{d}{dt}(\log y(t)) dt = [\log y(t)]_0^t = \log y(t) - \log A = \log \left(\frac{y(t)}{A} \right),$$

where we have used the fundamental theorem of calculus, aka Barrow's rule. Finally, we get the expected evolution

$$y(t) = e^{-\kappa t} A.$$

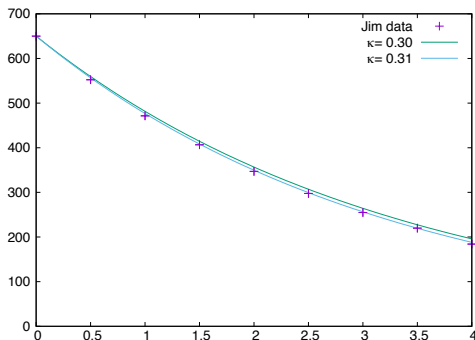
Observations:

- most of the differential equations can not be solved by hand, and one can use numerical methods;
- global features of the systems can be studied by using qualitative rather than quantitative approach.

Example. Jim has participated in a clinical analysis in order to test the effects of two tablets of acetaminophen in his body. The results of the analysis are shown in the following table:

Time (h)	0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0
Acetaminophen (mg)	650.0	552.3	471.5	406.7	347.1	297.6	254.9	219.8	184.2

Problem. We want to test the exponential decay behavior $y(t) = e^{-\kappa t} A$ of the drug clearance in Jim's body.



From the data, we see that the model describes qualitatively the drug clearance in Jim's body.

It seems that the standard value $\kappa = 0.30$ underestimates the decay, and that we can guess that $\kappa = 0.31$ is a better value.

That is, drug clearance in Jim's body is faster than average people.

Can we get a better value for κ ?

Abstract setting: We have data (t_i, y_i) for $i = 1, 2, \dots, N$. We should have $y_i = e^{-\kappa t_i} A$, where A is the initial dose, for a certain κ .

Parameter κ is non-linear, but it can be made linear just taking logarithms. So we should check if

$$\log(A/y_i) = \kappa t_i.$$

Optimality criterion: Look for κ minimizing the *residual sum of squares*

$$RSS(\kappa) = \sum_{i=1}^N (\log(A/y_i) - \kappa t_i)^2.$$

It is a second order polynomial in κ , that attains its minimum value at

$$\kappa = \frac{\sum_{i=1}^N t_i \log(A/y_i)}{\sum_{i=1}^N t_i^2}$$

In the present example, the result is $\kappa \simeq 0.3130$.

Population dynamics is the branch of life sciences that studies the size and age composition of populations as dynamic systems, and the biological and environmental processes driving them (such as birth and death rates, migrations, ...).

Several simple models for the size x of a biological population:

- Malthus' model, or equation of normal reproduction:

$$\dot{x} = \kappa x, \quad \kappa > 0.$$

The rate of reproduction is proportional (with constant κ) to the number of organisms present.

- Verhulst's model, or logistic equation:

$$\dot{x} = ax - bx^2, \quad a > 0, b > 0.$$

The competition of food leads to a decrease of the rate of reproduction, with $\kappa = a - bx$.

- Logistic growth with emigration:

$$\dot{x} = ax - bx^2 - c, \quad a > 0, b > 0, c > 0.$$

It includes the effect of the emigration at a constant rate c .

In the study of emigration, the control parameter is c .

Equilibrium states are found by solving equation

$$ax - bx^2 - c = 0,$$

leading to

$$x_{\pm} = \frac{a \pm \sqrt{a^2 - 4bc}}{2b}.$$

The value $c_* = \frac{a^2}{4b}$ is the *bifurcation*, at which the systems changes its qualitative behaviour:

- For $c < c_*$ the system has two equilibria: x_- is unstable and x_+ is stable;
- For $c = c_*$ the systems has a unique semistable equilibrium $x_* = \frac{a}{2b}$;
- For $c > c_*$ the system does not have equilibria and goes to extinction in a finite lapse of time.

The previous model can be applied also to the study of harvesting (for instance, we catch fish of a pond at a constant rate).

We have observed the dramatic changes produced if we harvest too much.

A presumably better way of harvesting is taking a rate proportional to the population. The model is

$$\dot{x} = ax - bx^2 - px, \quad a > 0, b > 0, p > 0.$$

This is in fact a logistic model, written as

$$\dot{x} = (a - p)x - bx^2.$$

In order to preserve the population, we take $p < a$.

The limiting value of the population is $x_+ = \frac{a-p}{b}$.

Observation: Bifurcation analysis let us to study the different possible behaviours of a system with respect to certain control parameters, so we can tune them appropriately to get a desired effect.

Continuity

Continuity

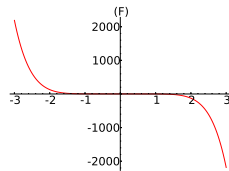
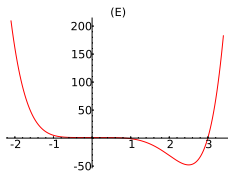
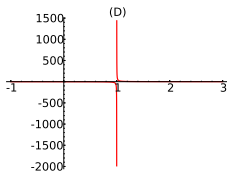
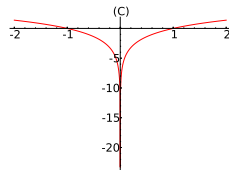
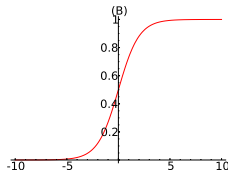
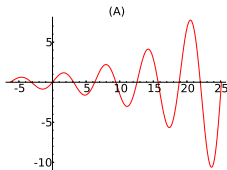
- Definition (the concept of limit).
- Examples: elementary functions.
- Properties: sum, product, composition.

Resources: Geogebra calculus applets at

<http://webspace.ship.edu/msrenault/GeoGebraCalculus/GeoGebraCalculusApplets.html>, by Marc Renault.

Example: match the elementary function

- (a) $x^6 - 3x^5 + 1$, (b) $1/(x - 1)$, (c) $\ln(x^2)$,
(d) $\exp(x/10) \sin(x)$, (e) $1/(1 + \exp(-x))$, (f) $-x^7 + 2$.



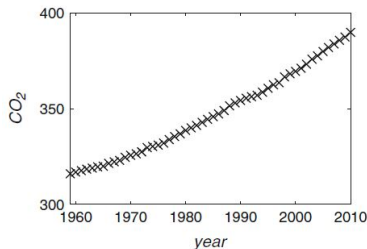
Derivatives of one-variable real functions

Atmospheric carbon dioxide concentration

Mean annual atmospheric carbon dioxide concentration at Mauna Loa observatory in Hawaii:

Year	1960	1965	1970	1975	1980	1985	1990
Average CO ₂	316.91	320.04	325.68	331.08	338.68	345.87	354.16

Year	1995	2000	2005	2007	2008	2009	2010
Average CO ₂	360.63	369.40	379.78	383.72	385.57	387.36	389.78



Source: [Ledder]

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Average rate period 1960–1970:

$$\frac{\Delta y}{\Delta t} = \frac{325.68 - 316.91}{1970 - 1960} \approx 0.877$$

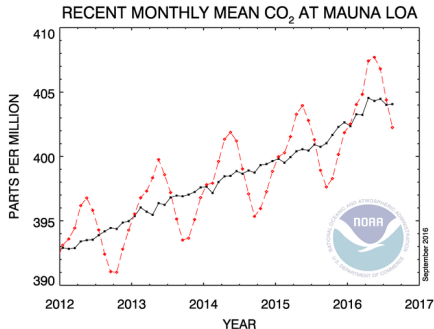
Average rate period 2005–2010:

$$\frac{\Delta y}{\Delta t} = \frac{389.78 - 379.78}{2010 - 2005} \approx 2.000$$

Atmospheric carbon dioxide concentration

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Average CO ₂	316.91	320.04	325.68	331.08	338.68	345.87	354.16

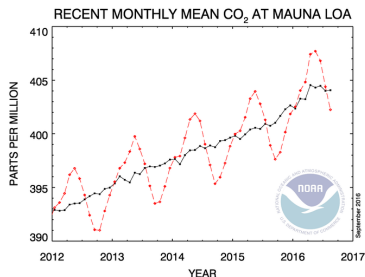
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Source: www.esrl.noaa.gov/gmd/ccgg/trends/

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- In many biological processes, either observed quantities or time units are **continuous**. Even though the number of molecules may be discrete, the chemical masses, biomasses, . . . can be assumed continuous.
- We must find a way to understand the **rate of change of continuous quantities over continuous time**.

Difference quotients

In the example given in Lecture 1 (acetaminophen), we had a model for the amount $y(t)$ of a drug in a human body at a time t :

$$y(t) = A e^{-\kappa t},$$

where A, κ are parameters.

The rate of change, for instance between $t = 0$ and a given $t = h$, would be

$$\frac{y(h) - y(0)}{h} = \frac{A e^{-\kappa h} - A}{h} = A \frac{e^{-\kappa h} - 1}{h}.$$

h	1.0	0.1	0.01	0.001	0.0001	0.00001	0.000001
$\Delta y / \Delta h$	-168.47	-192.10	-194.71	-194.97	-195.00	-195.00	-195.00

Table with $A = 650$ and $\kappa = 0.3$, working with 16 significant digits (we only show 5).

We would say that the **instantaneous rate** is **-195.00**.

Difference quotients

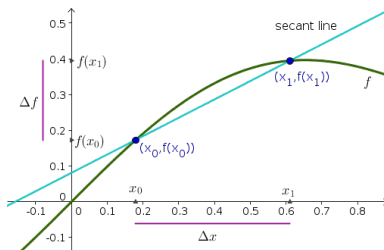
Let $f(x)$ be a continuous function defined on $D \subseteq \mathbb{R}$.

We define the **difference quotient** for $x, x_0 \in D$ as

$$\frac{\Delta f}{\Delta x}(x, x_0) = \frac{f(x) - f(x_0)}{x - x_0}$$

(In the previous example, $\frac{\Delta y}{\Delta t}(t, h) = \frac{y(t+h) - y(t)}{h}$.)

This corresponds to the concepts of **secant**, **mean velocity** and, in general, a **rate of change/average variation** of the function f along the interval $< x, x_0 > \dots$ and also a way to obtain **numerical derivatives**.



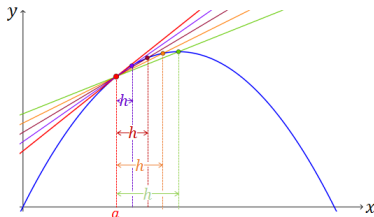
Derivatives

We define the **derivative of f at $x_0 \in D$** as

$$f'(x_0) := \frac{df(x)}{dx}(x_0) := \lim_{x \rightarrow x_0} \frac{f(x) - f(x_0)}{x - x_0}.$$

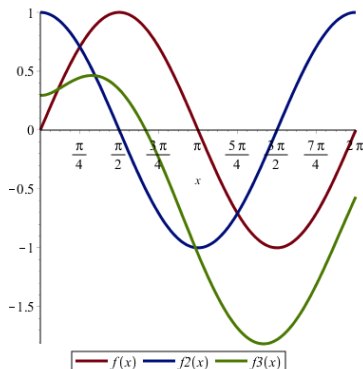
(In the previous example, $y'(t) = \frac{dy}{dt}(t) = \lim_{h \rightarrow 0} \frac{y(t+h) - y(t)}{h}$.)

It corresponds to the concepts of **tangent**, **instantaneous velocity** and, in general, the **instantaneous variation** of the function f at the point x_0 . Note that it involves the concept of limit.



The derivative as a function

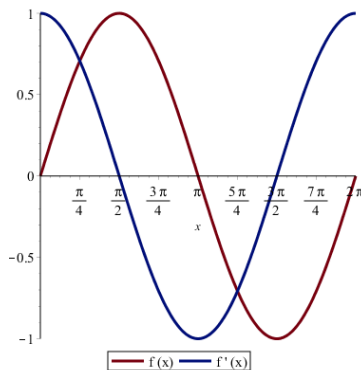
When the limit $f'(x)$ exists for all $x \in D \subseteq \mathbb{R}$ (D open), we say that f is **differentiable on D** . We can, then, consider f' as a new function defined on D :



Which curve is $f'(x)$? And $-f''(x)$?

The derivative as a function

When the limit $f'(x)$ exists for all $x \in D \subseteq \mathbb{R}$ (D open), we say that f is **differentiable on D** . We can, then, consider f' as a new function defined on D :



Derivatives in biology

We will find derivatives in many problems, mainly:

- Optimization problems in one and more variables.
- Differential equations (from the previous lecture):
 - Law of decay of a drug quantity: $\dot{y}(t) = -\kappa y(t)$.
 - Malthus-Verhulst-**logistic with emigration** laws in population dynamics:

$$\dot{x} = ax - bx^2 - c, \quad a > 0, b > 0, c > 0.$$

Computing derivatives

- Elementary derivative formulas.
- General derivative rules.

Remark: Using elementary derivative formulas and general derivative rules we can differentiate any function given explicitly.

Computing derivatives

Elementary derivative formulas

$f(x)$	x^p ($p \neq 0$)	e^{ax}	$\log x$	$\sin ax$	$\cos ax$	$\arctan(x/a)$	$\arcsin(x/a)$
$f'(x)$	$p x^{p-1}$	$a e^{ax}$	$\frac{1}{x}$	$a \cos ax$	$-a \sin ax$	$\frac{a}{a^2 + x^2}$	$\frac{1}{\sqrt{a^2 - x^2}}$
$f''(x)$							

Remark: To obtain the row of first derivatives, one has to use *equivalent infinitesimals*:

$$\lim_{x \rightarrow 0} \frac{e^x - 1}{x} = 1, \quad \lim_{x \rightarrow 0} \frac{\log(1+x) - 1}{x} = 1, \quad \lim_{x \rightarrow 0} \frac{\sin x}{x} = 1, \quad \lim_{x \rightarrow 0} \frac{1 - \cos x}{x} = 0.$$

Exercise: Complete the last row (using also general derivative rules).

Computing derivatives

General derivative rules

Let f and g be differentiable functions and a and b real constants.

- Sum: $[a f(x) + b g(x)]' = a f'(x) + b g'(x)$;
- Product: $[f(x) g(x)]' = f'(x) g(x) + f(x) g'(x)$;
- Quotient: $\left[\frac{f(x)}{g(x)} \right]' = \frac{f'(x) g(x) - f(x) g'(x)}{g(x)^2}$;
- Chain rule: $[f(g(x))]' = f'(g(x)) g'(x)$.

Exercise: If you feel *out of practice* with derivatives, do the “Check your understanding” boxes from the Ledder book’s section 1.3.3 and the Problems from 1.3.3 to 1.3.30. You can use tools like <http://www.derivative-calculator.net/> or <http://www.wolframalpha.com/calculators/derivative-calculator/> or ... to check the results.

The chain rule: interpretation I

The **chain rule** is an essential technique in mathematical modeling.

Example:

- t time;
- x position of any point along the rod (measured from hot end).
- $s(t)$ location of insect on the x axis;
- $T(x)$ temperature at any point on the rod;
- $u(t)$ temperature at insect's location.

Clearly, $u(t) = T(s(t))$; we want to know du/dt at some instant t_1 , assuming that we know $s(t)$ and $T(x)$ for any time (and so, their derivatives).

Let $x_1 = s(t_1)$. Insect's position changes as Δx in a small amount of time; using linear approximation (see below):

$$\Delta x \approx \frac{ds}{dt}(t_1) \Delta t.$$

The chain rule: interpretation II

On the other hand, insect's location temperature changes approximately as:

$$\Delta u \approx \frac{dT}{dx}(s(t_1)) \frac{ds}{dt}(t_1) \Delta t.$$

Dividing by Δt :

$$\frac{\Delta u}{\Delta t} \approx \frac{dT}{dx}(s(t_1)) \frac{ds}{dt}(t_1).$$

In the limit $\Delta t \rightarrow 0$,

$$\frac{du}{dt}(t_1) = \frac{dT}{dx}(s(t_1)) \frac{ds}{dt}(t_1).$$

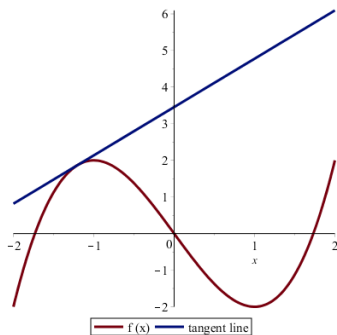
Since $u = T(s(t))$ and $x = s(t)$, we can write it in terms of variables as:

$$\frac{du}{dt} = \frac{du}{dx} \frac{dx}{dt}.$$

Tangent line

Since we seek for a straight line passing through $(x_0, f(x_0))$ and the slope must be $f'(x_0)$, then the **tangent line** to a graph $y = f(x)$ at a point $(x_0, f(x_0))$ is given by

$$y = f(x_0) + f'(x_0)(x - x_0).$$

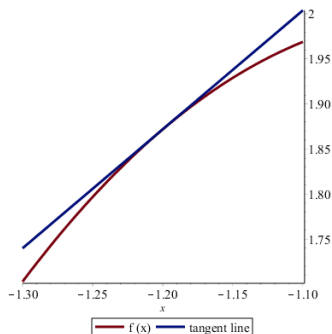


Tangent line to the graph of $x^3 - 3x$ at $x = -1.2$.

Tangent line

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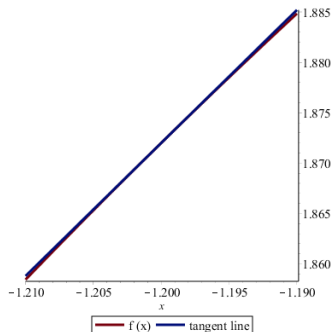


Tangent line to the graph of $x^3 - 3x$ at $x = -1.2$. Zoom 1.

Tangent line

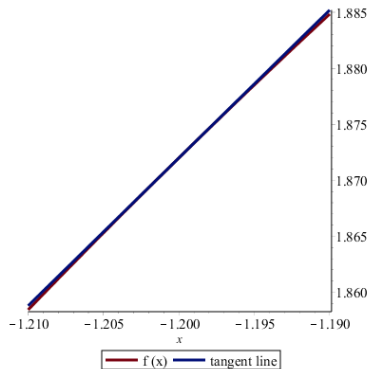
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$$y = f(x_0) + f'(x_0)(x - x_0).$$



Tangent line to the graph of $x^3 - 3x$ at $x = -1.2$. Zoom 2.

Linear approximation



Tangent line to the graph of $x^3 - 3x$ at $x = -1.2$. Zoom 2.

$$y = f(x_0) + f'(x_0)(x - x_0) \approx f(x)$$

Close to x_0 , taking $\Delta x = x - x_0$ and $\Delta f = f(x) - f(x_0)$, we have that

$$\Delta f \approx f'(x_0) \Delta x \quad \text{Linear Approximation}$$

Function growth and extrema

- If $f'(x_0) = 0$, then the tangent line is

$$y = f(x_0) + 0(x - x_0) \equiv f(x_0).$$

- A **local extremum** of a continuous function f is a point x_0 where f' changes sign.
- A **critical point** of a continuous function f is a point x_0 where $f'(x_0) = 0$ or $f'(x_0)$ does not exist.
- If f is differentiable, $f'(x_0) = 0$ is a necessary condition for x_0 to be a local extremum, but not sufficient.
- The local behavior of a function f near a point x_0 is determined by the lowest order derivative whose value is not zero, provided such a nonzero derivative exists.
- **Remark:** If f is differentiable, $f'(x_0) = 0$ and $f''(x_0) > 0$, then x_0 is a **local minimum**; if f is differentiable, $f'(x_0) = 0$ and $f''(x_0) < 0$, then x_0 is a **local maximum**.

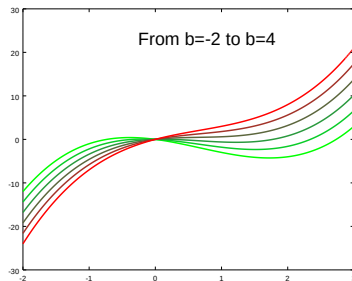
Function growth and extrema

Example:

$$f(x) = x^3 - 2x^2 + bx.$$

Octave script

```
x = -2:0.01:3;  
iMax=5  
bIni=-2  
bFin=4  
for i=0:iMax  
    b=bIni+i*(bFin-bIni)/iMax;  
    c=i/iMax;  
    plot(x,x.^3-2*x.^2+b*x,"Color",[c*c,1-c,c*(1-c)],"linewidth",2);  
    hold on  
end  
hold off
```



Global extrema

- Suppose x^* yields the largest or smallest value of a continuous function $f(x)$ on an interval $a \leq x \leq b$. Then either x^* is a critical point, $x^* = a$ or $x^* = b$.

Example: Fitness of gene pool

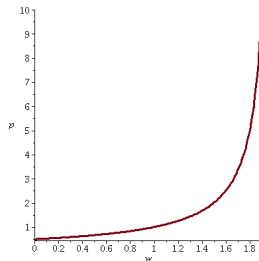
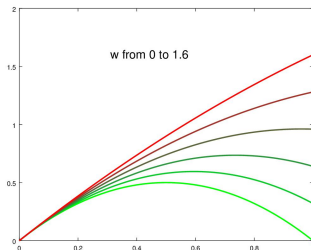
The gene responsible for sickle cell disease has two possible alleles, A and a . Individuals with the aa genotype have sickle cell anemia. Under natural conditions, people with sickle cell anemia did not live long enough to have children. Since the gene reduces fitness (adaptability), one would expect it to have been eliminated by natural selection. Indeed, people whose ancestors come from cold climates do not have the a allele, but this allele is not uncommon in parts of Africa. Individuals with the Aa genotype have a higher natural resistance to malaria than individuals with the AA genotype; where malaria is endemic, individuals with the Aa genotype have a longer life expectancy, which means they are likely to have more surviving children. Thus, the a allele has an indirect benefit along with its direct liability. To model the population dynamics of the sickle cell gene, let p be the fraction of A genes in the gene pool. We assume that the fitness of the aa genotype is 0, the fitness of the Aa genotype is 1, and the fitness of the AA genotype is a parameter w . According to the theory of genetics, the **overall fitness of the gene pool** is...

$$F(p) = w p^2 + 2 p (1 - p) = \dots = 2 p + (w - 2) p^2.$$

Example: Fitness of gene pool

$$F(p) = w p^2 + 2 p(1 - p) = \dots = 2 p + (w - 2) p^2.$$

- $F(0) = 0$; $F(1) = w$; $p^* = 1/(2 - w)$ critical point.
 $F(p^*) = p^* = 1/(2 - w)$.

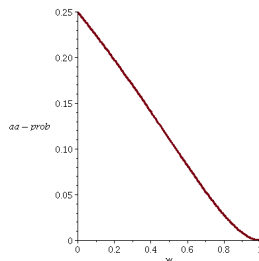
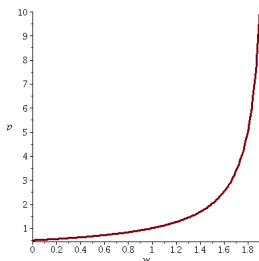


(Left) Graph for different w . (Right) Critical point in terms of w .

Example: Fitness of gene pool

$$F(p) = w p^2 + 2 p(1 - p) = \dots = 2 p + (w - 2) p^2.$$

- $F(0) = 0$; $F(1) = w$; $p^* = 1/(2 - w)$ critical point.
 $F(p^*) = p^* = 1/(2 - w)$.
- Conclusion: $w \geq 1 \Rightarrow$ disappearance of the sickle cell trait (all AA, free of malaria).
- Conclusion: $w < 1 \Rightarrow$ the sickle cell trait (a remains, malaria endemic) with aa-probability of $(1 - w)^2/(2 - w)^2$.



(Left) Critical point in terms of w . (Right) Survival probability of the sickle cell trait.

Application: The marginal value theorem

Imagine a process occurring at **different patches** (in general, locations) and consisting of **collecting** something **with increasing difficulty**.



Apples from different trees



Distributed parallel computing



Animals foraging at different food sources

Trade-off:

- It costs some time to move from one tree to the next, which suggests that you should stay longer at the first tree.
- However, the apples get harder to pick as time goes on, which suggests that you should move to a new tree sooner.

Goal:

- Find the right amount of **perseverance** (evolutionary advantages).

Application: The marginal value theorem

Let $f(t)$ the **net resource gain** in one patch as a function of time.

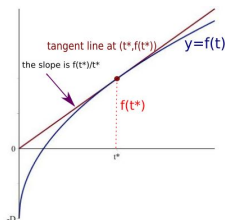
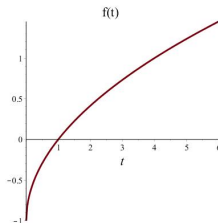
Typically, it has the following properties

- $f(0) < 0$, to account for the resources used up in the process of changing patches.
- $f'(t) > 0$, $f''(t) < 0$ to account for an increasing foraging that loses efficiency along time.

We want to **maximize** the net resource gain relative to the time spent in each patch:

$$f(t)/t$$

A **necessary condition** is that $f'(t) = \frac{f(t)}{t}$.



Application: The marginal value theorem

Let $f(t)$ the **net resource gain** in one patch as a function of time.

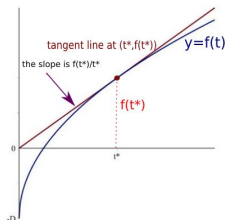
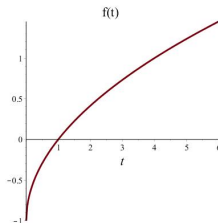
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- $f'(t) > 0$, $f''(t) < 0$ to account for an increasing foraging that loses efficiency along time.

We want to **maximize** the net resource gain relative to the time spent in each patch, $f(t)/t$.

A **necessary condition** to attain this maximum at t^* is that

$$f'(t^*) = \frac{f(t^*)}{t^*}.$$

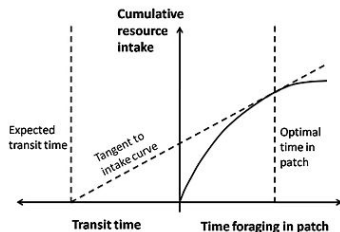


Application: The marginal value theorem

Let $f(t)$ the **net resource gain** in one patch as a function of time with

- $f(0) < 0$, $f'(t) > 0$, $f''(t) < 0$ to account for the resources used up in the process of changing patches and an increasing foraging that loses efficiency along time.

A **necessary condition** (indeed, also sufficient¹) for $f(t)/t$ to attain this maximum at t^* is that $f'(t^*) = \frac{f(t^*)}{t^*}$.



¹ Prove that $(f(t^*)/t^*)'' = f''(t^*)/t^3$

Numerical solution of equations

Problem:

An equimolecular mix of carbon monoxide and oxygen reaches the equilibrium at temperature $T = 300^\circ\text{K}$ and pressure $P = 5 \text{ atm}$. The theoretical chemical reaction is $\text{CO} + \frac{1}{2}\text{O}_2 \rightleftharpoons \text{CO}_2$, while the real chemical reactions is $\text{CO} + \text{O}_2 \rightarrow x\text{CO} + \frac{1}{2}(1+x)\text{O}_2 + (1-x)\text{CO}_2$, where x is the fraction of remaining CO. The equation for equilibrium that determines the fraction x is:

$$K_p = \frac{(1-x)(3+x)^{1/2}}{x(x+1)^{1/2}P^{1/2}}, \quad 0 < x < 1,$$

where $K_p = 3.06$ is the equilibrium constant for such temperature and pressure.

Question: Which is the value of x ?

A zero or a root of a function f is an element x_0 of its domain such that $f(x_0) = 0$. That is, x_0 is a solution of the equation $f(x) = 0$.

In general, f is a vector-valued function, that is, $f(x) = 0$ is a system of n equations and n unknowns $x = (x_1, \dots, x_n)$.

Goal: Compute the solutions of equations $f(x) = 0$.

Methodology: Three steps:

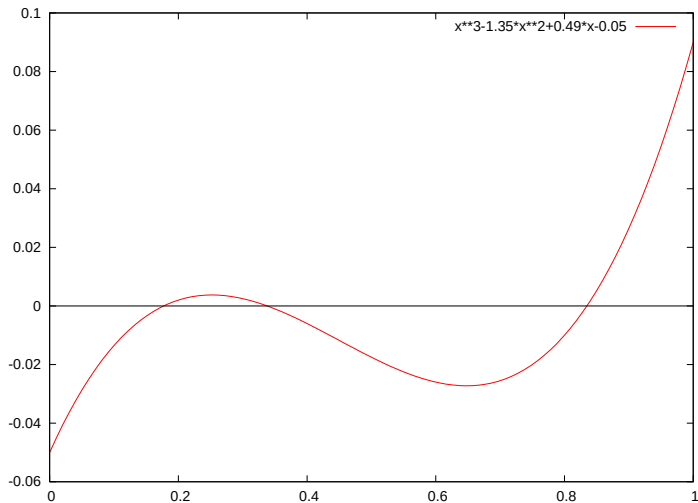
- 1 Localization:** Find domains that have the zeroes.
- 2 Separation:** Find domains that have only one zero.
- 3 Approximation:** Compute a sequence of approximations converging to the zero.

Here: $n = 1$.

Zeroes of functions

An example

4



$$f(x) = x^3 - 1.35 x^2 + 0.49 x - 0.05$$

Bolzano's theorem

Let $f : [a, b] \rightarrow \mathbb{R}$ be a continuous function such that $f(a)f(b) < 0$. Then, there exists $\alpha \in]a, b[$ such that $f(\alpha) = 0$.

Proof: The proof is based on the bisection method, which is an iterative process that produces a sequence intervals converging to a point, in this case a zero of the function. The corresponding algorithm is as follows:

- 0) Take $[a_0, b_0] = [a, b]$, $n = 0$.
- 1) At step n , the interval $[a_n, b_n]$ is such that $f(a_n)f(b_n) < 0$, and compute $c_{n+1} = (a_n + b_n)/2$.
- 2) There are three alternatives:
 - $f(c_{n+1}) = 0$, so $\alpha = c_{n+1}$ and stop the iterative process;
 - $f(a_n)f(c_{n+1}) < 0$, and then take $[a_{n+1}, b_{n+1}] = [a_n, c_{n+1}]$;
 - $f(c_{n+1})f(b_n) < 0$, and the take $[a_{n+1}, b_{n+1}] = [c_{n+1}, b_n]$.
- 3) Repeat step 1) for step $n + 1$.

If the iteration stops is due to the fact we have found α .

Otherwise, we construct a sequence of nested intervals

$$[a, b] = [a_0, b_0] \supset [a_1, b_1] \supset \dots \supset [a_n, b_n] \supset \dots,$$

whose lengths go to 0.

Since the sequence $(a_n)_n$ is increasing, and bounded from above, it has a limit, say α . Analogously, since the sequence $(b_n)_n$ is decreasing, and bounded from below, then it has also a limit, β .

Since

$$0 = \lim_{n \rightarrow \infty} (b_n - a_n) = \beta - \alpha,$$

then $\beta = \alpha$.

At this point we use the continuity property of the function f , so that

$$\lim_{n \rightarrow \infty} f(a_n) = \lim_{n \rightarrow \infty} f(b_n) = f(\alpha).$$

Since $f(a_n)f(b_n) < 0$ for all n , then,

$$0 \geq \lim_{n \rightarrow \infty} f(a_n)f(b_n) = f(\alpha)^2.$$

But this is only possible if $f(\alpha) = 0$.



- Bolzano's theorem is a tool for **localizing** zeroes of functions.
- In order to prove the uniqueness of a zero in a certain interval, we usually use arguments involving the monotonicity of the function.
- The mathematical **proof** of Bolzano's theorem provides a computational method to approximate the zero of a function: the bisection method.
- From a theoretical point of view, the iterative process usually never stops.
- From the practical point of view, one usually stops the process when gets enough accuracy in the approximation of the zero, that is when $|f(c_n)|$ or $b_n - a_n$ are below a certain **tolerance**.
- The bisection method is always **convergent**.

Example: We want to solve equation $f(x) = \exp(x - 0.5) - 2x + 0.35$.

1) Study of the function.

Since $f'(x) = \exp(x - 0.5) - 2$, then function f has an unique local extremum at $x_m = \log(2) + .5 \simeq 1.19315$. In fact:

- f is stricly decreasing at $] - \infty, x_m[$;
- f is stricly increasing at $]x_m, +\infty[$;
- x_m is a global minimum, with $f(x_m) = 1.35 - 2 \log(2) \simeq -0.0362944 < 0$.

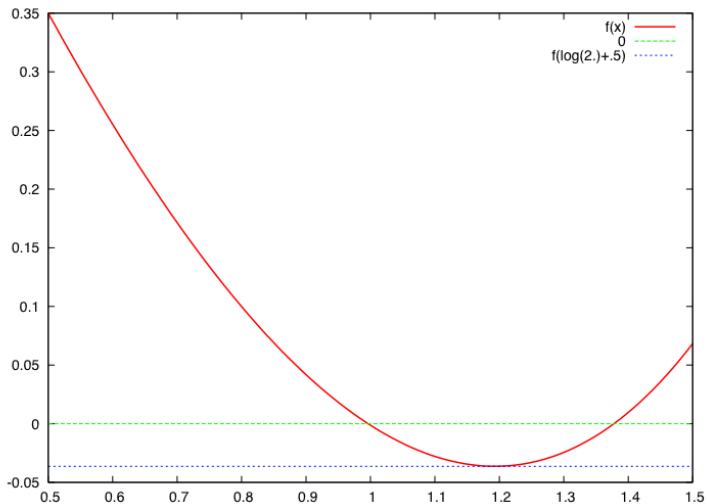
Moreover, since $\lim_{x \rightarrow -\infty} f(x) = +\infty$ and $\lim_{x \rightarrow +\infty} f(x) = +\infty$, llavors

- f has one zero α_1 at $] - \infty, x_m[$;
- f has one zero α_2 at $]x_m, +\infty[$;
- α_1 and α_2 are the zeroes of f .

Example: the equation $\exp(x - 0.5) - 2x + 0.35 = 0$

Graphical representation

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2) Computation of α_1 (with 8 figures): $\alpha_1 = 0.99639033$

n	a_n	b_n	$b_n - a_n$	$f(a_n)$	$f(b_n)$	c_{n+1}	$f(c_{i+1})$
0	0.950000000	1.050000000	1.0e-01	1.8e-02	-1.7e-02	1.000000000	-1.3e-03
1	0.950000000	1.000000000	5.0e-02	1.8e-02	-1.3e-03	0.975000000	8.0e-03
2	0.975000000	1.000000000	2.5e-02	8.0e-03	-1.3e-03	0.987500000	3.2e-03
3	0.987500000	1.000000000	1.2e-02	3.2e-03	-1.3e-03	0.993750000	9.5e-04
4	0.993750000	1.000000000	6.2e-03	9.5e-04	-1.3e-03	0.996875000	-1.7e-04
5	0.993750000	0.996875000	3.1e-03	9.5e-04	-1.7e-04	0.995312500	3.9e-04
6	0.995312500	0.996875000	1.6e-03	3.9e-04	-1.7e-04	0.996093750	1.1e-04
7	0.996093750	0.996875000	7.8e-04	1.1e-04	-1.7e-04	0.996484375	-3.4e-05
8	0.996093750	0.996484375	3.9e-04	1.1e-04	-3.4e-05	0.996289063	3.6e-05
9	0.996289063	0.996484375	2.0e-04	3.6e-05	-3.4e-05	0.996386719	1.3e-06
10	0.996386719	0.996484375	9.8e-05	1.3e-06	-3.4e-05	0.996435547	-1.6e-05
11	0.996386719	0.996435547	4.9e-05	1.3e-06	-1.6e-05	0.996411133	-7.4e-06
12	0.996386719	0.996411133	2.4e-05	1.3e-06	-7.4e-06	0.996398926	-3.1e-06
13	0.996386719	0.996398926	1.2e-05	1.3e-06	-3.1e-06	0.996392822	-8.9e-07
14	0.996386719	0.996392822	6.1e-06	1.3e-06	-8.9e-07	0.996389771	2.0e-07
15	0.996389771	0.996392822	3.1e-06	2.0e-07	-8.9e-07	0.996391296	-3.5e-07
16	0.996389771	0.996391296	1.5e-06	2.0e-07	-3.5e-07	0.996390533	-7.3e-08
17	0.996389771	0.996390533	7.6e-07	2.0e-07	-7.3e-08	0.996390152	6.3e-08
18	0.996390152	0.996390533	3.8e-07	6.3e-08	-7.3e-08	0.996390343	-5.3e-09
19	0.996390152	0.996390343	1.9e-07	6.3e-08	-5.3e-09	0.996390247	2.9e-08
20	0.996390247	0.996390343	9.5e-08	2.9e-08	-5.3e-09	0.996390295	1.2e-08
21	0.996390295	0.996390343	4.8e-08	1.2e-08	-5.3e-09	0.996390319	3.2e-09
22	0.996390319	0.996390343	2.4e-08	3.2e-09	-5.3e-09	0.996390331	-1.0e-09
23	0.996390319	0.996390331	1.2e-08	3.2e-09	-1.0e-09	0.996390325	1.1e-09
24	0.996390325	0.996390331	6.0e-09	1.1e-09	-1.0e-09	0.996390328	1.1e-09

Problem: Let x_0 be an approximate zero of f . How could we improve the estimate?

(Assume we know f').

Let h be the correction of x_0 , so that the new approximation is $x_1 = x_0 + h$. Then, we would like

$$0 = f(x_0 + h) \approx f(x_0) + f'(x_0)h.$$

Then, we choose

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

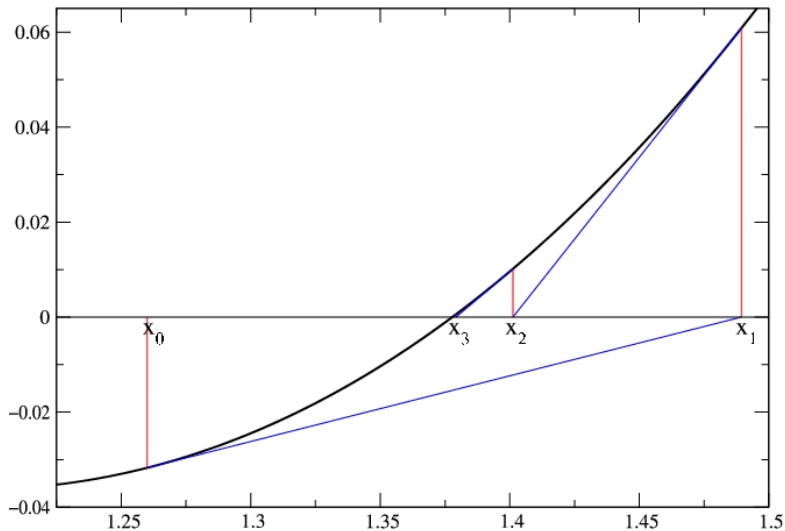
Newton's method (aka known Newton–Raphson method) consists in, given an initial approximation x_0 of a root of f , generate the sequence of approximations $(x_n)_n$, by the recurrence:

$$x_{n+1} = x_n - \frac{f(x_n)}{f'(x_n)}, \quad n = 0, 1, \dots$$

Newton's method

Geometrical idea

12



- Newton's method is not always convergent.
- There is a convergence theorem: the **Newton-Kantorovich** theorem.
- If the method converges, the convergence uses to be very fast.
- The method uses derivatives.
- In the implementations of the method, one usually stops the iteration when $|x_{n+1} - x_n| < \varepsilon$ or $|f(x_{n+1})| < \delta$, on $\varepsilon > 0, \delta > 0$ are error tolerances.
- The method can be generalized to work with nonlinear systems of equations.

Example: the equation $\exp(x - 0.5) - 2x + 0.35 = 0$

Application of Newton's method

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We compute α_1 , zero of $f(x) = \exp(x - 0.5) - 2x + 0.35$ at $[0.95, 1.05]$, with Newton's method, from initial value $x_0 = 0.95$.

n	x_n	$f(x_n)$	$f'(x_n)$	$ x_n - x_{n-1} $
0	0.950000000000	1.8312185490e-02	-4.3168781451e-01	
1	0.99241997313	1.4312185890e-03	-3.6372883516e-01	0.4e-01
2	0.99635482363	1.2683863782e-05	-3.5727766888e-01	0.4e-02
3	0.99639032504	1.0352153579e-09	-3.5721934888e-01	0.4e-04
4	0.99639032794	1.1102230246e-16	-3.5721934412e-01	0.3e-08

Problem: Let x_0, x_1 be approximate zeroes of f . How could we improve the estimate?

Let h be the correction of x_1 to obtain the new approximation $x_2 = x_1 + h$. Then, we want

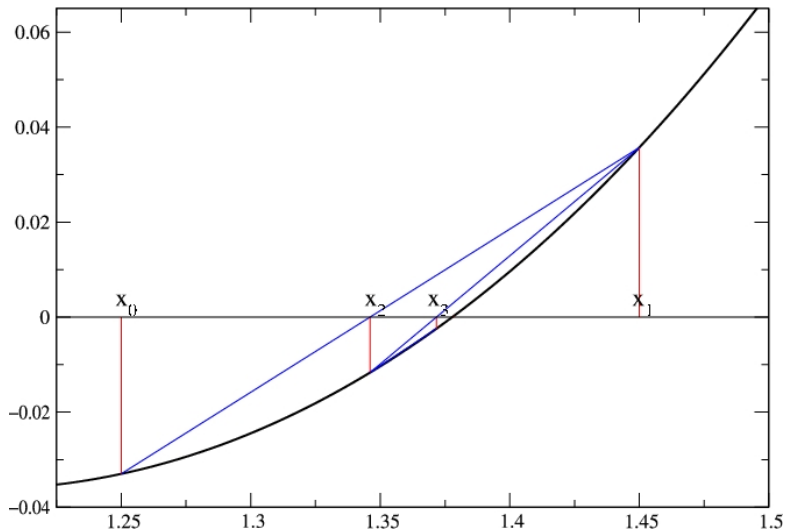
$$0 = f(x_1 + h) \approx f(x_1) + f'(x_1)h \approx f(x_1) + \delta f(x_0, x_1) h ,$$

where $\delta f(x_0, x_1) = \frac{f(x_1) - f(x_0)}{x_1 - x_0}$. Hence, we take

$$h = -\frac{f(x_1)}{\delta f(x_0, x_1)} .$$

Secant method consist in, given two different approximations of a root, generate a sequence of approximations $(x_n)_n$, given by

$$x_{n+1} = x_n - f(x_n) \frac{x_n - x_{n-1}}{f(x_n) - f(x_{n-1})} , \quad n = 1, 2, \dots$$



- Secant method is not always convergent.
- There is a convergence theorem.
- If the method converges, the convergence is fast, but not as fast as Newton's method.
- The method does not use derivatives.
- In the implementations of the method, one usually stops the iteration when $|x_{n+1} - x_n| < \varepsilon$ or $|f(x_{n+1})| < \delta$, on $\varepsilon > 0, \delta > 0$ are error tolerances.
- The method can be generalized to work with nonlinear systems of equations (quasi-Newton's methods).

Example: the equation $\exp(x - 0.5) - 2x + 0.35 = 0$

Application of secant method

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We compute α_1 , zero of $f(x) = \exp(x - 0.5) - 2x + 0.35$ at $[0.95, 1.05]$, with secant method, from initial value $x_0 = 0.95$, $x_1 = 1.05$.

n	x_n	$f(x_n)$	$\delta f(x_{n-1}, x_n)$	$ x_n - x_{n-1} $
0	9.5000000000e-01	1.8312185490e-02		
1	1.0500000000e+00	-1.6746982133e-02	-3.5059167623e-01	0.1e+00
2	1.0022322312e+00	-2.0587539114e-03	-3.0749244921e-01	0.5e-01
3	9.9553693212e-01	3.0544752958e-04	-3.5311364194e-01	0.7e-02
4	9.9640194410e-01	-4.1494063644e-06	-3.5791057710e-01	0.9e-03
5	9.9639035069e-01	-8.1245864481e-09	-3.5720978398e-01	0.2e-04
6	9.9639032794e-01	2.1704860131e-13	-3.5721932772e-01	0.3e-07
7	9.9639032794e-01	2.1704860131e-13	-3.5721932772e-01	0.0

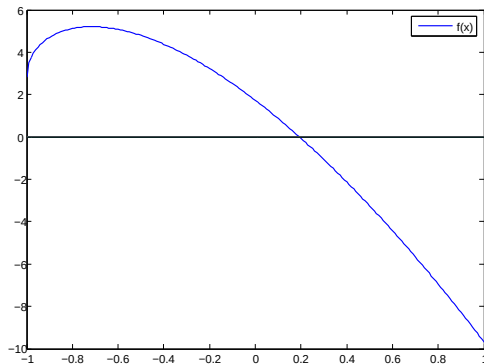
We are asked to solve equation

$$K_p = \frac{(1-x)(3+x)^{1/2}}{x(x+1)^{1/2}P^{1/2}}, \quad 0 < x < 1,$$

where $K_p = 3.06$ and $P = 5$.

This is equivalent to find the zeroes of function

$$f(x) = (1-x)\sqrt{3+x} - K_p\sqrt{P}x\sqrt{1+x}$$



Using Newton's method from $x_0 = 0$:

n	x_n	$f(x_n)$	$f'(x_n)$
0	0.0000000e+00	1.7320508e+00	-8.2857437e+00
1	2.0903987e-01	-1.5582646e-01	-9.7446356e+00
2	1.9304886e-01	-8.3948986e-04	-9.6394777e+00
3	1.9296178e-01	-8.6179369e-08	-9.6389027e+00
4	1.9296177e-01	5.7451469e-08	-9.6389027e+00
5	1.9296177e-01	5.7451469e-08	-9.6389027e+00

Result: $x \simeq 0.1929617704785 \dots$

The problem of the chemical equilibrium

Using Newton's method (other possible choices)

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We could also look for the unique zero at the interval $[0, 1]$ of the polynomial function $f(x) = (PK_p^2 - 1)x^3 + (PK_p^2 - 1)x^2 + 5x - 3$.

Using Newton's method from $x_0 = 0$.

n	x_n	$f(x_n)$	$f'(x_n)$
0	0.0000000e+00	-3.0000000e+00	5.0000000e+00
1	6.0000002e-01	2.6391169e+01	1.0946504e+02
2	3.5890782e-01	6.8148637e+00	5.5594986e+01
3	2.3632728e-01	1.3453506e+00	3.4332970e+01
4	1.9714189e-01	1.1747546e-01	2.8407431e+01
5	1.9300650e-01	1.2435187e-03	2.7806711e+01
6	1.9296178e-01	1.9213077e-07	2.7800241e+01
7	1.9296178e-01	1.9213077e-07	2.7800241e+01

Using Newton's method from $x_0 = 0.5$

n	x_n	$f(x_n)$	$f'(x_n)$
0	5.0000000e-01	1.6681749e+01	8.5181496e+01
1	3.0416229e-01	4.0489445e+00	4.5588730e+01
2	2.1534771e-01	6.5910071e-01	3.1107981e+01
3	1.9416019e-01	3.3420280e-02	2.7973827e+01
4	1.9296549e-01	1.0334284e-04	2.7800777e+01
5	1.9296178e-01	1.9213077e-07	2.7800241e+01
6	1.9296178e-01	1.9213077e-07	2.7800241e+01

We look for the unique zero at $[0, 1]$ of the function

$f(x) = (1 - x)\sqrt{3 + x} - K_p\sqrt{P}x\sqrt{1 + x}$, using secant method with $x_0 = 0$ and $x_1 = 1$.

n	x_n	$f(x_n)$	$\delta f(x_{n-1}, x_n)$
0	0.0000000e+00	1.7320508e+00	
1	1.0000000e+00	-9.6765690e+00	-1.1408620e+01
2	1.5181950e-01	3.9093074e-01	-1.1869525e+01
3	1.8475516e-01	7.8879923e-02	-9.4745569e+00
4	1.9308060e-01	-1.1454452e-03	-9.6121454e+00
5	1.9296144e-01	3.2173295e-06	-9.6392937e+00
6	1.9296177e-01	5.7451469e-08	-9.6389017e+00
7	1.9296177e-01	5.7451469e-08	-9.6389017e+00

Polynomial interpolation

An example: the antifreeze

2

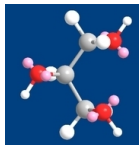
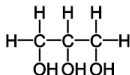
Statement of the problem

"Glycerin has lots of uses besides being used to make nitroglycerin. Some uses for glycerin include: conserving preserved fruit, as a base for lotions, to prevent freezing in hydraulic jacks, to lubricate molds, in some printing inks, in cake and candy making, and (because it has an antiseptic quality) sometimes to preserve scientific specimens in jars in your high school biology lab."

Goal: We want to estimate the freezing point of an antifreeze consisting of a solution of glycerin and water at a 45% concentration level in weight.

Data. We have a table of values (taken from previous experiments) with the values of the freezing point (in Celsius degrees) (y), as a function of the concentration of glycerin (x).

x	0	10	20	30	40	50	60	70	80	90	100
y	0	-1.6	-4.8	-9.5	-15.4	-21.9	-33.6	-37.8	-19.1	-1.6	17



Glycerol: Molecular representation and 3D model showing the atoms and a pair of

Interpolating the points by means of a suitable function, like a polynomial $p(x)$, we can estimate the freezing point when $x = 45\%$ from $p(45)$. We are free to choose more or less points from the table. For instance, if we consider the closest ones, we get:

x	30	40	50	60
y	-9.5	-15.4	-21.9	-33.6

Since we have 4 pairs of data, we look for $p(x) = a_0 + a_1x + a_2x^2 + a_3x^3$ such that

$$p(30) = -9.5, \quad p(40) = -15.4, \quad p(50) = -21.9, \quad p(60) = -33.6.$$

We end up with the system (with unknowns a_0, a_1, a_2, a_3)

$$\begin{cases} a_0 + a_1 30 + a_2 30^2 + a_3 30^3 &= -9.5, \\ a_0 + a_1 40 + a_2 40^2 + a_3 40^3 &= -15.4, \\ a_0 + a_1 50 + a_2 50^2 + a_3 50^3 &= -21.9, \\ a_0 + a_1 60 + a_2 60^2 + a_3 60^3 &= -33.6, \end{cases}$$

and we obtain $a_0 = 50.6$, $a_1 = -3.98\bar{3}$, $a_2 = 0.089$, $a_3 = -0.0007\bar{6}$.

An example: the antifreeze

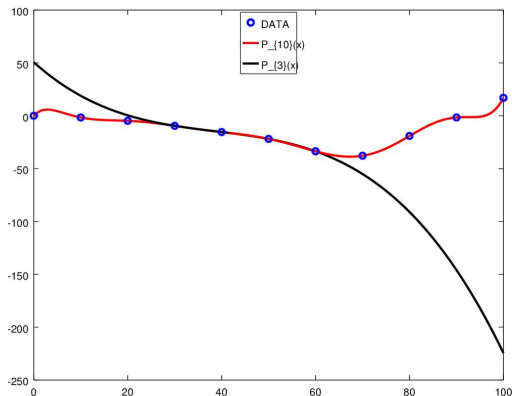
4

Possible solution

We finally obtain the polynomial

$$p(x) = 50.60 - 3.98\bar{3}x + 0.0890x^2 - 0.0007\bar{6}x^3$$

and so the approximate freezing-point value is $p(45) \approx -18.3$ Celsius degrees.

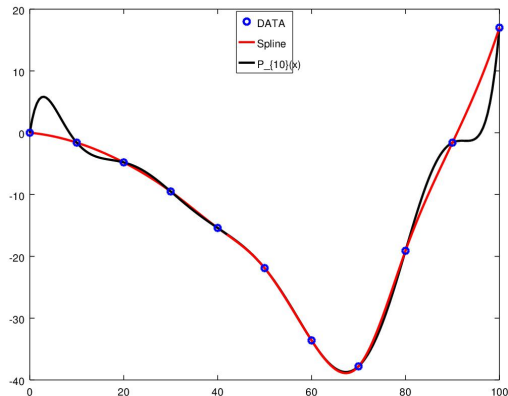


An example: the antifreeze

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Possible solution

In the previous plot, we can appreciate that the approximation fails at the ends. To improve this failure, there are other interpolation schemes, like *splines*:



Theorem: Given $n + 1$ points $(x_0, y_0), (x_1, y_1), \dots, (x_n, y_n)$, with all nodes $x_0, x_1, \dots, x_n$ different, there exists a unique polynomial $p_n(x)$ of degree less or equal than n , such that

$$p_n(x_i) = y_i, \quad i = 0, 1, 2, \dots, n.$$

Proof: Let

$$p_n(x) = a_0 + a_1x + a_2x^2 + \dots + a_nx^n$$

the desired interpolating polynomial, whose has $n + 1$ coefficients must fulfill the following $n + 1$ -equation **linear system**:

$$\begin{cases} a_0 + a_1x_0 + a_2x_0^2 + \dots + a_nx_0^n &= y_0 \\ a_0 + a_1x_1 + a_2x_1^2 + \dots + a_nx_1^n &= y_1 \\ \dots & \\ a_0 + a_1x_n + a_2x_n^2 + \dots + a_nx_n^n &= y_n \end{cases}$$

The interpolating polynomial

Existence and uniqueness theorem (end of proof)

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The determinant of the system is

$$\Delta = \begin{vmatrix} 1 & x_0 & \dots & x_0^n \\ 1 & x_1 & \dots & x_1^n \\ \vdots & \vdots & \dots & \vdots \\ 1 & x_n & \dots & x_n^n \end{vmatrix} = \prod_{\substack{i,j=0, \\ i>j}}^n (x_i - x_j) .$$

Since $\Delta \neq 0$ by hypothesis, the system is compatible and determined. Therefore, the problem **has a solution** and **it is unique**.

Remark: Δ is called the *Vandermonde determinant*.

Remark: The proof also provides a *direct (but inefficient) algorithm* to compute the interpolating polynomial.

Idea: The $n + 1$ *Lagrange polynomials*

$$l_k(x) = \frac{(x - x_0) \cdots (x - x_{k-1})(x - x_{k+1}) \cdots (x - x_n)}{(x_k - x_0) \cdots (x_k - x_{k-1})(x_k - x_{k+1}) \cdots (x_k - x_n)} ,$$

where $k = 0, \dots, n$, form a base of the vector space of polynomials of degree $\leq n$, and satisfy

$$l_k(x_i) = \delta_{ik} = \begin{cases} 1 & \text{si } i = k \\ 0 & \text{si } i \neq k \end{cases} .$$

Application: The interpolating polynomial is, then,

$$p_n(x) = \sum_{k=0}^n y_k l_k(x) .$$

Example: Consider the following table of values of a function f

x	30	40	50	60
y	-9.5	-15.4	-21.9	-33.6

We want to estimate $f(45)$ using a polynomial of degree 3.

1) The Lagrange polynomials are:

$$l_0(x) = \frac{-1}{6000}(x-40)(x-50)(x-60),$$

$$l_1(x) = \frac{1}{2000}(x-30)(x-50)(x-60),$$

$$l_2(x) = \frac{-1}{2000}(x-30)(x-40)(x-60),$$

$$l_3(x) = \frac{1}{6000}(x-30)(x-40)(x-50).$$

2) The interpolating polynomial is

$$\begin{aligned} p_3(x) = & \frac{9.5}{6000}(x-40)(x-50)(x-60) \\ & - \frac{15.4}{2000}(x-30)(x-50)(x-60) \\ & + \frac{21.9}{2000}(x-30)(x-40)(x-60) \\ & - \frac{33.6}{6000}(x-30)(x-40)(x-50) . \end{aligned}$$

3) Finally: $f(45) \approx p_3(45) = -18.2875 \approx -18.3$.

Question: To extrapolate one result from a table of values, how many nodes do we have to consider?

Answer: We can increment the number of nodes since the extrapolated value stabilizes.

Remark: It seems reasonable to take more interpolation nodes in order to improve the estimations. The following example illustrates some inherent problems . . .

Example: In order to estimate the valor $f(45)$ corresponding to the freezing point of the antifreeze at 45% of glycerin:

- nodes 40 – 50, $p_1(45) = -18.6500 \approx -18.7$;
- nodes 30 – 60, $p_3(45) = -18.2875 \approx -18.3$;
- nodes 20 – 70, $p_5(45) = -18.1457 \approx -18.1$;
- nodes 10 – 80, $p_7(45) = -18.1234 \approx -18.1$;
- nodes 00 – 90, $p_9(45) = -18.1363 \approx -18.1$.

Thus, it seems reasonable to approximate $f(45) \approx -18.1$.

Remark: The value 45 occupies a “central” place within the table.

Example: In order to estimate the valor $f(85)$ corresponding to the freezing point of the antifreeze at 85% of glycerin:

- nodes 80 – 90, $p_1(85) = -10.35$;
- nodes 70 – 100, $p_3(85) = -10.3437 \dots \approx -10.34$;
- nodes 50 – 100, $p_5(85) = -8.9528 \approx -8.95$;
- nodes 30 – 100, $p_7(85) = -7.6172 \approx -7.62$;
- nodes 10 – 100, $p_9(85) = -7.1235 \approx -7.12$.

Idea: Express the interpolating polynomial of $\{(x_0, y_0), \dots, (x_n, y_n)\}$ in the form:

$$p_n(x) = c_0 + c_1(x - x_0) + \dots + c_n(x - x_0)(x - x_1) \cdots (x - x_{n-1}) .$$

We have

$$y_0 = p_n(x_0) = c_0$$

$$y_1 = p_n(x_1) = c_0 + c_1(x_1 - x_0) = y_0 + c_1(x_1 - x_0)$$

$$y_2 = p_n(x_2) = c_0 + c_1(x_2 - x_0) + c_2(x_2 - x_0)(x_2 - x_1)$$

...

and so

$$c_0 = y_0, \quad c_1 = \frac{y_1 - y_0}{x_1 - x_0}, \quad c_2 = \frac{\frac{y_2 - y_1}{x_2 - x_1} - \frac{y_1 - y_0}{x_1 - x_0}}{x_2 - x_0}, \dots$$

We compute *divided differences*

$$\begin{array}{l|l}
 x_0 & f[x_0] = y_0 = c_0 \\
 & f[x_0, x_1] = \frac{f[x_1] - f[x_0]}{x_1 - x_0} = c_1 \\
 x_1 & f[x_1] = y_1 \\
 & f[x_1, x_2] = \frac{f[x_2] - f[x_1]}{x_2 - x_1} \\
 x_2 & f[x_2] = y_2 \\
 & \vdots \\
 & \vdots \\
 & f[x_{n-1}, x_n] = \frac{f[x_n] - f[x_{n-1}]}{x_n - x_{n-1}} \\
 x_n & f[x_n] = y_n
 \end{array}
 \quad
 \begin{array}{l}
 \\
 \\
 f[x_0, x_1, x_2] = \frac{f[x_1, x_2] - f[x_0, x_1]}{x_2 - x_0} = c_3 \\
 \\
 \dots
 \end{array}$$

Then: $c_j = f[x_0, x_1, \dots, x_j]$ per $j = 0, 1, \dots, n$.

Example: Consider the following table of values of a function f

x	30	40	50	60
y	-9.5	-15.4	-21.9	-33.6

We want to estimate $f(45)$ using a polynomial of degree 3.

1) The table of divided differences is

30	-9.5			
		$\frac{-15.4+9.5}{40-30} = -0.59$		
40	-15.4		$\frac{-0.65+0.59}{50-30} = -0.003$	
		$\frac{-21.9+15.4}{50-40} = -0.65$		$\frac{-0.026+0.003}{60-30} = -0.00076$
50	-21.9		$\frac{-1.17+0.65}{60-40} = -0.026$	
		$\frac{-33.6+21.9}{60-50} = -1.17$		
60	-33.6			

2) The interpolating polynomial, $p_3(x)$, is

$$\begin{aligned} p_3(x) = & -9.5 - 0.59(x - 30) \\ & -0.003(x - 30)(x - 40) \\ & -0.00076(x - 30)(x - 40)(x - 50) . \end{aligned}$$

3) Finally: $f(45) \approx p_3(45) = -18.2875$.

Theorem: Let f be a function with all its first $n + 1$ derivatives continuous in the interval $[a, b]$, and let M_{n+1} be an upper bound of $|f^{(n+1)}(x)|$ in $[a, b]$.

Let p_n be the interpolating polynomial of f on a given set of $(n + 1)$ nodes $x_0, x_1, \dots, x_n \in [a, b]$ such that $p_n(x_i) = f(x_i)$, $i = 0, 1, 2, \dots, n$.

Then, for all $x \in [a, b]$ there exists a $\xi_x \in [a, b]$ such that

$$f(x) - p_n(x) = \frac{f^{(n+1)}(\xi_x)}{(n+1)!} (x - x_0) \cdots (x - x_n),$$

and

$$|f(x) - p_n(x)| \leq \frac{M_{n+1}}{(n+1)!} |(x - x_0) \cdots (x - x_n)|.$$

- **Extreme value theorem:** A continuous function $f(x)$ on a closed interval $[a, b]$ must attain a **maximum** and a **minimum** at least once. In other words, there exist numbers c_{max} and c_{min} in $[a, b]$ such that

$$f(c_{min}) \leq f(x) \leq f(c_{max}) \quad \text{for all } x \in [a, b].$$

- **Corollary:** Given a continuous function $f(x)$ on a closed interval $[a, b]$, there exist real numbers m and M such that

$$m \leq f(x) \leq M \quad \text{for all } x \in [a, b].$$

- **Mean value theorem:** If a function f is continuous on the $[a, b]$, where $a < b$, and differentiable on the interval (a, b) , then there exists a point $c \in \text{in}(a, b)$ such that

$$f'(c) = \frac{f(b) - f(a)}{b - a}.$$

- **Corollary (Rolle's theorem):** If, in addition, $f(a) = f(b)$, then $\dots f'(c) = 0$.

We define the error at each point as $R_n(x) := f(x) - p_n(x)$, and construct the auxiliary function

$$Y(t) = R_n(t) - \frac{R_n(x)}{W(x)} W(t),$$

where $W(u) = \prod_{i=0}^n (u - x_i)$.

Since x_i are roots of $f - p_n$, we have $Y(x_i) = 0$ and so Y has $n + 2$ roots. From Rolle's theorem, $Y'(t)$ has $n + 1$ roots and, inductively, we finally have that $Y^{(n+1)}(t)$ has one root $\xi \in (a, b)$. Moreover, since p_n is a polynomial of degree n ,

$$Y^{(n+1)}(t) = R_n^{(n+1)}(t) - \frac{R_n(x)}{W(x)} (n+1)! = f^{(n+1)}(t) - \frac{R_n(x)}{W(x)} (n+1)!$$

Therefore,

$$Y^{(n+1)}(\xi) = f^{(n+1)}(\xi) - \frac{R_n(x)}{W(x)} (n+1)! = 0$$

and

$$R_n(x) = f(x) - p_n(x) = \frac{f^{(n+1)}(\xi)}{(n+1)!} \prod_{i=0}^n (x - x_i)$$

- 1 The error at the interpolation nodes is zero.
- 2 If $f(x)$ is a polynomial of degree n , the error is zero everywhere.
- 3 **General bounds:**

If $a = x_0 \leq x_1 \leq \dots \leq x_n = b$, and $|f^{(n+1)}(x)| \leq M_{n+1}$ for all $x \in [a, b]$, then:

$$|f(x) - p_n(x)| \leq \frac{M_{n+1}}{(n+1)!} (b-a)^{n+1}.$$

- 4 **Specific bounds** (equally spaced nodes):

If $x_i = x_0 + i \cdot h$ for $i = 0, 1, \dots, n$, with $h = \frac{(b-a)}{n}$, and $|f^{(n+1)}(x)| \leq M_{n+1}$ for all $x \in [a, b]$, then:

$$|f(x) - p_n(x)| \leq \frac{M_{n+1}}{4(n+1)} \left(\frac{b-a}{n} \right)^{n+1}.$$

Example: We interpolate the functions sinus and cosinus in the interval $[0, \frac{\pi}{2}]$ for a polynomial of degree 6, using equally spaces nodes. Which is the truncating error?

Solution: Both for $f(x) = \sin x$ and $f(x) = \cos x$, we can bound any derivative (in particular, the 7th one) by 1. Then, at any point $x \in [0, \frac{\pi}{2}]$, we can bound the truncating error by

$$|f(x) - p_6(x)| \leq \frac{1}{4 \cdot 7} \left(\frac{\pi/2}{6} \right)^7 \leq 3.02 \cdot 10^{-6}.$$

Exercise: How many equally spaced nodes (and so, which degree of the interpolating polynomial) are needed for the truncating error at any point in the interval $[0, \frac{\pi}{2}]$ to be less than 10^{-10} ?

Answer: 11 nodes (degree 10) since the value of $\frac{1}{4(n+1)} \left(\frac{\pi}{2n} \right)^{(n+1)}$ for $n = 9$ is still of order 10^{-9} but for $n = 10$ it is 0.3×10^{-10} .

Question: Does the approximation obtained with the interpolating polynomial improves when we increase the number of nodes (and so the degree of p_n)?

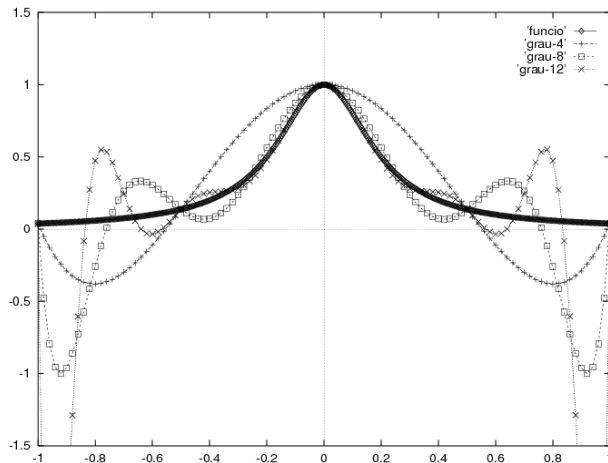
Example: (C. Runge(1901)) Let $p_n(x)$ the interpolating polynomial of the function

$$f(x) = \frac{1}{1 + 25x^2}, \quad x \in [-1, 1],$$

on the set of equally spaced points $x_i = -1 + \frac{2i}{n}$, $i = 0, 1, \dots, n$.

Then, if $0.726 \dots \leq |x| < 1$, $\sup_{n \geq 0} |f(x) - p_n(x)| = \infty$.

Remark: The error near the origin is small but nearby -1 and 1 it grows with n .



We observe the function $f(x) = 1/(1 + 25x^2)$ and its interpolating polynomials of degrees 4, 8 and 12.

Taylor polynomials and power series

Example: The *virial*¹ *expansion* or *virial series* of a gas is its state equation in the form

$$Z := \frac{PV}{nRT} = 1 + B_2(T) \left(\frac{n}{V} \right) + B_3(T) \left(\frac{n}{V} \right)^2 + \dots$$

where P is the *pressure*, V is the *volume*, T is the *absolute temperature*, n is the *number of moles*, and $R \simeq 8.3145 \text{ J K}^{-1} \text{ mol}^{-1}$ is the *ideal gas constant*.

Z is the compressibility factor (for an ideal gas, $Z = 1$).

The addends are successive corrections to the ideal case, and correspond to intramolecular forces between pairs ($B_2(T)$), triplets ($B_3(T)$), and so on.

Other forms of the virial equation use the *molar volume* $\bar{V} = V_m := V/n$ or the *molar density* $\rho := n/V$. In the latter²,

$$\frac{P}{RT} = \rho + B_2(T)\rho^2 + B_3(T)\rho^3 + \dots$$

¹From latin, “virial” means “force”. Here refers the fact that gases are not ideal since there are intramolecular forces.

²The equation was proposed in 1901 by the Nobel laureate Heike Kamerlingh

An example: real gases

Virial coefficients: experimental data

3

Coefficients 1, B_2 , B_3 , etc. are the *virial coefficients* (at a certain temperature), and can be obtained from experiments and from theoretical models of *statistical mechanics*.

In this table it is shown the *second virial coefficient* (B_2) for several gases, at $T = 300$ K.

Gas	$B_2(300)$
ammonia	-265
argon	-16
carbon dioxide	-126
chlorine	-299
ethylene	-139
hydrogen	15
methane	-43
nitrogen	-4
oxygen	-16
sulfur hexafluoride	-275
water	-1126

Source: W.M. Haynes (ed.) *CRC Handbook of Chemistry and Physics*, 97a ed., Boca Raton (Florida), CRC Press 2016.

Problem: How can we compute the virial expansion from a given state equation, obtained theoretically from the intramolecular potential of a gas?

An important example is the *Van der Waals equation of state*:

$$\left(P + a \left(\frac{n}{V} \right)^2 \right) (V - nb) = nRT,$$

where a and b are gas dependent constants.

The *second virial coefficient* $B_2(T)$ is the most important, since it is the main correction term.

The *Boyle temperature* is the temperature for which the *second virial coefficient* is zero, that is T_B such that $B_2(T_B) = 0$. At this temperature, the gas behaves as if it were ideal.

Problem: Which is the Boyle temperature for the Van der Waals equation of state?

Definition: The **Taylor polynomial of order n of a smooth function f at a point x_0** of its domain is a polynomial that matches the value of the function f and the first n derivatives at the point x_0 , and it is given by the formula:

$$\begin{aligned} p_n(x, x_0) &= f(x_0) + f'(x_0)(x - x_0) + \frac{f''(x_0)}{2!}(x - x_0)^2 + \cdots + \frac{f^{(n)}(x_0)}{n!}(x - x_0)^n \\ &= \sum_{k=0}^n \frac{f^{(k)}(x_0)}{k!}(x - x_0)^k . \end{aligned}$$

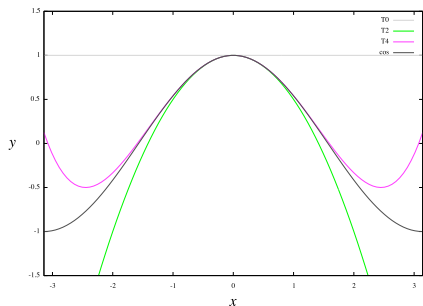
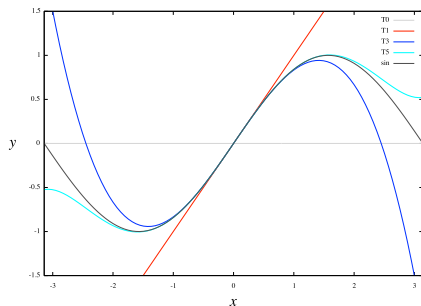
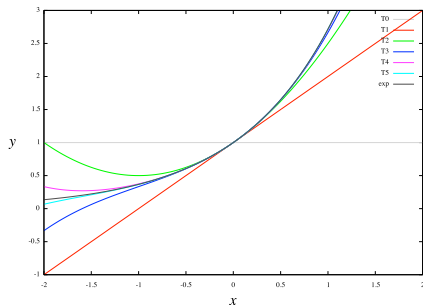
Remark: The Taylor polynomial of order n is a local approximation (of order n) of the function f .

The Taylor polynomial

Examples

6

Taylor polynomials for the functions
 $f(x) = e^x$, $f(x) = \sin x$, $f(x) = \cos x$ at the point 0.



Theorem: Let $f :]a, b[\rightarrow \mathbb{R}$ be a $(n + 1)$ times differentiable function, and $x_0 \in]a, b[$. Let

$$r_n(x, x_0) = f(x) - p_n(x, x_0)$$

be the **remainder** or **truncation error** at a point $x \in]a, b[$. Then, there exists $\xi_x \in]x_0, x[$ such that

$$r_n(x, x_0) = \frac{f^{(n+1)}(\xi_x)}{(n+1)!} (x - x_0)^{n+1}.$$

Example: We want to approximate sine and cosine functions using their Taylor polynomials of order 6, centered at 0. We also want to estimate the truncation error for any $x \in [0, \pi/2]$.

For the sine function, we have

$$p_6^s(x) = x - \frac{1}{3!}x^3 + \frac{1}{5!}x^5,$$

and the remainder is

$$|r_6^s(x)| = \frac{|\sin(\xi^s)|}{7!}x^7 \leq \frac{1}{7!}x^7.$$

For the cosine function, we have

$$p_6^c(x) = 1 - \frac{1}{2!}x^2 + \frac{1}{4!}x^4 - \frac{1}{6!}x^6,$$

and the remainder is

$$|r_6^c(x)| = \frac{|\cos(\xi^c)|}{7!}x^7 \leq \frac{1}{7!}x^7.$$

Taylor's theorem

An application in computer approximations of functions

9

For $x \in [0, \pi/2]$, we obtain the following bound for the remainders, in both the sine and cosine cases:

$$\frac{1}{7!} \left(\frac{\pi}{2}\right)^7 \leq 0.47 \cdot 10^{-2}.$$

Question: What is the order we have to reach in such a way that the truncation error is smaller than 10^{-10} ? Answer: 15.

If we “take” $n = \infty$ in the definition of the Taylor polynomial, we get

$$S(f)(x, x_0) = \sum_{k=0}^{\infty} \frac{f^{(k)}(x_0)}{k!} (x - x_0)^k,$$

which is the *Taylor series* or the *power series* of the function f at the point x_0 .

Remark: In order that $f(x) = S(f)(x, x_0)$, the remainder $r_n(x, x_0)$ has to go to zero when n goes to $+\infty$. A convergence criteria for general power series

$$S(f)(x, x_0) = \sum_{k=0}^{\infty} a_k (x - x_0)^k,$$

is as follows:

$$\text{If } \lim_{k \rightarrow \infty} \left| \frac{a_k}{a_{k+1}} \right| = R, \text{ the series } S(f)(x, x_0) \text{ converges for } x \text{ s.t.} \\ |x - x_0| < R.$$

In the Taylor case, $a_k = \frac{f^{(k)}(x_0)}{k!}$, and a posteriori $S(f)(x, x_0) = f(x)$ for x s.t. $|x - x_0| < R$.

$$\frac{1}{1-x} = \sum_{n=0}^{\infty} x^n = 1 + x + x^2 + x^3 + \cdots, \quad -1 < x < 1$$

$$(1+x)^\alpha = \sum_{n=0}^{\infty} \binom{\alpha}{n} x^n = 1 + \alpha x + \frac{\alpha(\alpha-1)}{2!} x^2 + \cdots, \quad \alpha \in \mathbb{R}, \quad -1 < x < 1$$

$$e^x = \sum_{n=0}^{\infty} \frac{x^n}{n!} = 1 + x + \frac{x^2}{2!} + \frac{x^3}{3!} + \cdots, \quad -\infty < x < \infty$$

$$\sin x = \sum_{n=0}^{\infty} (-1)^n \frac{x^{2n+1}}{(2n+1)!} = x - \frac{x^3}{3!} + \frac{x^5}{5!} - \frac{x^7}{7!} + \cdots, \quad -\infty < x < \infty$$

$$\cos x = \sum_{n=0}^{\infty} (-1)^n \frac{x^{2n}}{(2n)!} = 1 - \frac{x^2}{2!} + \frac{x^4}{4!} - \frac{x^6}{6!} + \cdots, \quad -\infty < x < \infty$$

$$\ln(1-x) = \sum_{n=1}^{\infty} \frac{-1}{n} x^n = -x - \frac{x^2}{2} - \frac{x^3}{3} - \frac{x^4}{4} + \cdots, \quad -1 < x < 1$$

$$\ln(1+x) = \sum_{n=1}^{\infty} \frac{(-1)^{n+1}}{n} x^n = x - \frac{x^2}{2} + \frac{x^3}{3} - \frac{x^4}{4} + \cdots, \quad -1 < x < 1$$

$$n! = 1 \cdot 2 \cdot \cdots \cdot n, \quad \binom{\alpha}{n} = \frac{\alpha(\alpha-1) \cdots (\alpha-n+1)}{n!}$$

Example: Compute the power series (at $x_0 = 0$) of the function

$$f(x) = \frac{1}{1-x} = (1-x)^{-1}.$$

Solution: We have that

$$f^{(k)}(x) = k!(1-x)^{-k-1}.$$

Therefore, $f^{(k)}(0) = k!$ and

$$S(f)(x) = \sum_{k=0}^{\infty} \frac{k!}{k!} x^k = \sum_{k=0}^{\infty} x^k = 1 + x + x^2 + \dots$$

The formula works for $-1 < x < 1$.

Power series

The geometric series

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x	0.2	-0.5	2
$f(x)$	1.25	$0.\hat{6}$	-1
$p_0(x)$	1.00000000	1.00000000	1
$p_1(x)$	1.20000000	5.00000000E-001	3
$p_2(x)$	1.24000000	7.50000000E-001	7
$p_3(x)$	1.24800000	6.25000000E-001	15
$p_4(x)$	1.24960000	6.87500000E-001	31
$p_5(x)$	1.24992000	6.56250000E-001	63
$p_6(x)$	1.24998400	6.71875000E-001	127
$p_7(x)$	1.24999680	6.64062500E-001	255
$p_8(x)$	1.24999936	6.67968750E-001	511
$p_9(x)$	1.24999988	6.66015625E-001	1023
$p_{10}(x)$	1.24999998	6.66992188E-001	2047
$p_{11}(x)$	1.25000000	6.66503906E-001	4095
$p_{12}(x)$	1.25000000	6.66748047E-001	8191
$p_{13}(x)$	1.25000000	6.66625977E-001	16383
$p_{14}(x)$	1.25000000	6.66687012E-001	32767
$p_{15}(x)$	1.25000000	6.66656494E-001	65535

Question: Which is the series for $x = 1/2$?

We can do algebraic operations with power series, as well as compose, compute derivatives and integrals.

Example 1: We want to compute the power series of the function

$$f(x) = \frac{1}{1 - 8x^3}.$$

Solution: Define $y = 8x^3$. We know that, for $-1 < y < 1$,

$$\frac{1}{1 - y} = \sum_{k=0}^{\infty} y^k.$$

Hence, if $-\frac{1}{2} < x < \frac{1}{2}$

$$\frac{1}{1 - 8x^3} = \sum_{k=0}^{\infty} (8x^3)^k = \sum_{k=0}^{\infty} 8^k x^{3k} = 1 + 8x^3 + 8^2 x^6 + \dots$$

Example 2: We want to compute the power series of the function

$$f(x) = \frac{1}{2} \log \left(\frac{1+x}{1-x} \right).$$

Solution 1: The series of $\log(1+x)$ and $\log(1-x)$ work for $-1 < x < 1$, and subtracting them and dividing by 2 we obtain:

$$\frac{1}{2} \log \left(\frac{1+x}{1-x} \right) = x + \frac{x^3}{3} + \frac{x^5}{5} + \frac{x^7}{7} + \dots$$

Solution 2: Differentiating $f(x)$, we obtain $f'(x) = \frac{1}{1-x^2}$, and, hence,

$$f'(x) = 1 + x^2 + x^4 + \dots$$

at the interval $-1 < x < 1$. By integrating the series (term by term) from 0 to x , and taking into account that $f(0) = 0$, we reach the same solution.

Application: To compute $\log z$ for any $z > 0$, one can compute first $x \in]-1, 1[$ such that $z = \frac{1+x}{1-x}$, that is $x = \frac{z-1}{z+1}$, and apply the previous formula.

Problem: Find the virial series of Van der Waals equation

$$\left(P + a \left(\frac{n}{V}\right)^2\right) (V - nb) = nRT,$$

and Boyle's temperature.

Solution: We have to expand with respect to the molar density $\rho = n/V$ the compressibility factor Z :

$$Z = \frac{PV}{nRT} = \frac{1}{1 - b\rho} - \frac{a}{RT} \left(\frac{n}{V}\right) = \frac{1}{1 - b\rho} - \frac{a}{RT}\rho.$$

If $-1 < b\rho < 1$, then:

$$Z = 1 + \left(b - \frac{a}{RT}\right)\rho + b^2\rho^2 + b^3\rho^3 + \dots$$

In particular $B_2(T) = \frac{\partial Z}{\partial \rho} \Big|_{\rho=0} = \left(b - \frac{a}{RT}\right)$

Boyle temperature is $T_B = \frac{a}{Rb}$.

Problem: Given a dipole with charges q i $-q$, at distance $2d$ of each other, what is the order of magnitude of the electric field of the corresponding dipole far away in a point in the axis?

Solution: If the charges $q, -q$ are at points $d, -d$, respectively, of X axis, the intensity of electric field generated by the dipole at a point x on the axis is

$$E = \kappa \left(\frac{q}{(x-d)^2} - \frac{q}{(x+d)^2} \right).$$

By hypothesis, $x \gg d$. By defining $u = \frac{d}{x} \ll 1$, we have

$$E = \kappa \frac{q}{x^2} \left(\frac{1}{(1-u)^2} - \frac{1}{(1+u)^2} \right).$$

From the binomial formula, we know that ³

$$\frac{1}{(1-u)^2} = 1 + 2u + 3u^2 + 4u^3 + \dots$$

Then,

$$\begin{aligned} E &= \kappa \frac{q}{x^2} ((1 + 2u + 3u^2 + 4u^3 + \dots) - (1 - 2u + 3u^2 - 4u^3 + \dots)) \\ &= \kappa \frac{q}{x^2} 2(2u + 4u^3 + \dots) \\ &= \kappa \frac{4qd}{x^3} (1 + 2u^2 + \dots) \end{aligned}$$

In summary, the intensity of the electric field at a point x far away of the dipole is approximately inversely proportional to the cube of the distance.

³One can also differentiate the series $\frac{1}{1-u} = 1 + u + u^2 + u^3 + \dots$

Problem: We want to compute

$$\int_0^1 \frac{\sin x}{x} dx,$$

but, unfortunately, the primitive of $f(x) = \frac{\sin x}{x}$ can not be expressed by means of elementary functions.

Solution: By integrating at interval $[0, x]$ the power series of $f(x)$, we obtain:

$$\int_0^x \frac{\sin x}{x} dx = \sum_{n=0}^{\infty} \frac{(-1)^n x^{2n+1}}{(2n+1) (2n+1)!}.$$

In particular,

$$\int_0^1 \frac{\sin x}{x} dx = \sum_{n=0}^{\infty} \frac{(-1)^n}{(2n+1) (2n+1)!}.$$

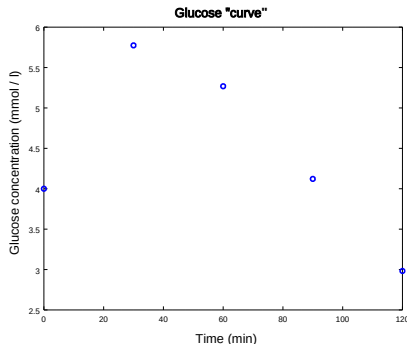
Integration in one variable

- **Recordings of glucose levels** are performed in diabetes control to get information about an individual's glucose tolerance. It is common practice to use simple summary measures: fasting value, two-hour (2-h) value or **area under the curve (AUC)**,...

t	0	30	60	90	120
y	4.00	5.77	5.27	4.12	2.98

Table shows OGTTs (oral glucose tolerance tests) with 5 glucose measurements over two hours recorded for healthy pregnant women in their first trimester (averages over population).

Goal: Compute the **area under the curve**.

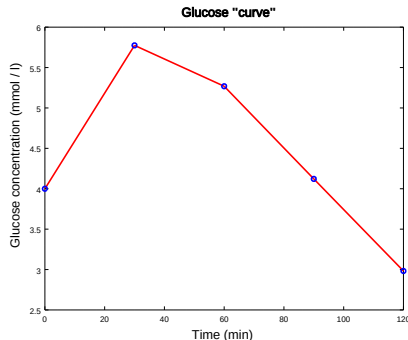


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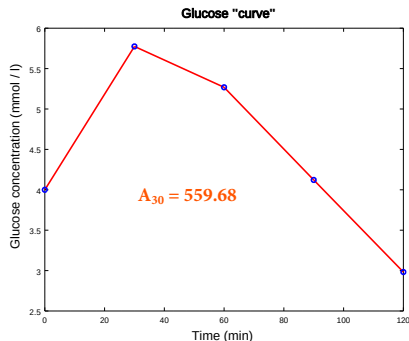
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- **Goal:** Compute the **area under the curve**.

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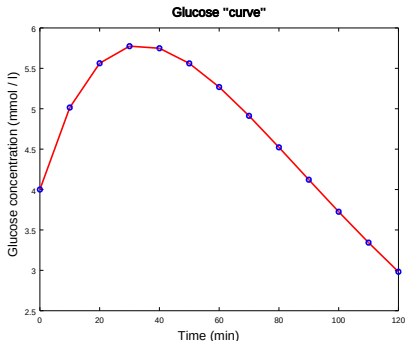
$$\begin{aligned} A \approx A_{30} &:= \frac{4.00 + 5.77}{2} 30 + \frac{5.77 + 5.27}{2} 30 + \frac{5.27 + 4.12}{2} 30 + \frac{4.12 + 2.98}{2} 30 \\ &= \frac{30}{2} (4.00 + 2 \cdot (5.77 + 5.27 + 4.12) + 2.98) = 559.68 \end{aligned}$$



- Assume that you have a non-invasive way to record glucose levels and you can take more measurements.

t	0	10	20	30	40	50	60	70	80	90	100	110	120
y	4.00	5.02	5.56	5.77	5.75	5.56	5.27	4.91	4.52	4.12	3.73	3.34	2.98

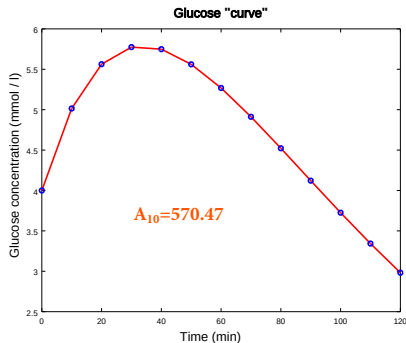
Table shows OGTTs (oral glucose tolerance tests) with 13 glucose measurements over two hours recorded for healthy pregnant women in their first trimester (averages over population).



- **Goal:** Compute the **area under the curve**.

t	0	10	20	30	40	50	60	70	80	90	100	110	120
y	4.00	5.02	5.56	5.77	5.75	5.56	5.27	4.91	4.52	4.12	3.73	3.34	2.98

$$A \approx A_{10} := \frac{10}{2} (4.00 + 2 \cdot (5.02 + 5.56 + 5.77 + 5.75 + 5.56 + 5.27 + 4.91 + 4.52 + 4.12 + 3.73 + 3.34) + 2.98) = 570.47$$



Heuristics: If we could take infinitely many measurements, we could get the area under the curve through a limiting process, taking finer partitions of the interval.

The area under the curve, defined with the limiting process, is the definite integral

$$A = \int_0^{120} y(t) dt.$$

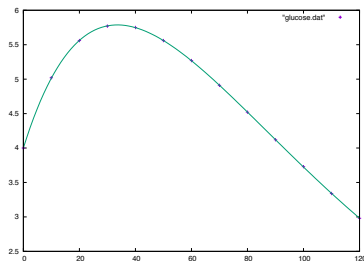
In fact, the values of the table have an excellent fit with the function

$$y(t) = (a + bt) \exp(-ct)$$

where

$$a \simeq 4.0014, \quad b \simeq 0.20549, \quad c \simeq 0.018858.$$

The area is $A \simeq 571.77$.



In general, given an independent variable z representing a **quantity** (time, length, volume, etc.), and a dependent variable representing some stuff f per unit of the quantity (a density), then the total stuff in a certain interval $[a, b]$ is the definite integral

$$\text{total stuff} = \int_a^b (\text{stuff per unit } \text{quantity}) dz.$$

We assume that $f(x)$ is a bounded function defined on $[a, b]$ and that $\{x_0, \dots, x_n\}$ is a partition (P) of $[a, b]$. For each i we let

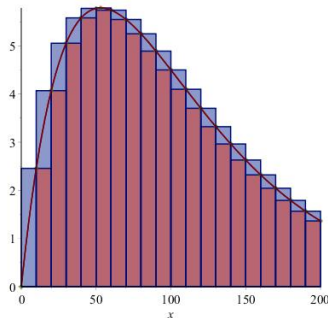
$$M_i(f) = \sup_{x \in [x_{i-1}, x_i]} f(x), \quad m_i(f) = \inf_{x \in [x_{i-1}, x_i]} f(x).$$

Letting $\Delta x_i = x_i - x_{i-1}$, the **upper and lower (Darboux) sums** of $f(x)$ with respect to the partition P are defined as

$$U(f, P) = \sum_{i=1}^n M_i(f) \Delta x_i,$$

$$L(f, P) = \sum_{i=1}^n m_i(f) \Delta x_i,$$

respectively.

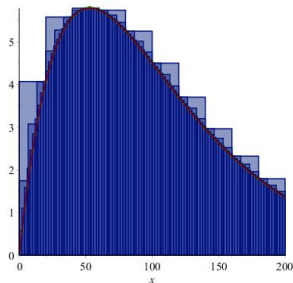


Comparison of the upper (blueish) and lower (reddish) Riemann sums for a fixed partition.

The **upper and lower integrals** of $f(x)$ on $[a, b]$ are defined as

$$U(f) = \inf(U(f, P)), \quad L(f) = \sup(L(f, P)),$$

respectively, where both the infimum and the supremum are taken over all possible partitions



Upper Riemann sums for a gradation of partitions.

Definition. If the **upper and lower integral of $f(x)$ are equal** to each other, their common value is denoted by

$$\int_a^b f(x) dx,$$

and is referred to as the **Riemann integral of f** .

Example 1:

$$\int_0^1 x^2 dx$$

Take $\Delta x = 1/n$:

$$\frac{1}{n} \sum_{k=0}^{n-1} \left(\frac{k}{n}\right)^2 \leq \int_0^1 x^2 dx \leq \frac{1}{n} \sum_{k=1}^n \left(\frac{k}{n}\right)^2$$

From Problem 2 in Exam Model, we know that $\sum_{k=1}^n k^2 = \frac{1}{3} n^3 + \frac{1}{2} n^2 + \frac{1}{6} n$, so:

$$\frac{1}{n^3} \left(\frac{1}{3} (n-1)^3 + \frac{1}{2} (n-1)^2 + \frac{1}{6} (n-1) \right) \leq \int_0^1 x^2 dx \leq \frac{1}{n^3} \left(\frac{1}{3} n^3 + \frac{1}{2} n^2 + \frac{1}{6} n \right).$$

Since both sides of the inequality tend to $\frac{1}{3}$ when n goes to ∞ , then

$$\int_0^1 x^2 dx = \frac{1}{3}.$$

Example 2: [Ledder, Example 1.7.6.]

Goal and strategy:

- We want to relate the **birth rate** of a population with **survival and fecundity** data in a female population.
- We will calculate the birth rate at time t by adding up the births to mothers of various ages.

Ingredients:

- $B(t)$ is the birth rate at time t .
- Take all possible mothers of age in $[a, a + da]$. Observe that they were born when the birth rate was $B(t - a)$. So, the initial size of this cohort was $B(t - a) da$.
- Let $\ell(a)$ be the fraction of individuals who survive to age a or greater. Then, the size of the age- a cohort is $\ell(a) B(t - a) da$.
- Let $a \in [a_1, a_2]$, the age-interval of fertility and $m(a)$ be the rate of births per capita for age- a individuals. Then the total rate of births for mothers of age a is $m(a) \ell(a) B(t - a) da$.

Thus, the **birth rate satisfies the equation**

$$B(t) = \int_{a_1}^{a_2} m(a) \ell(a) B(t - a) da.$$

Example 3: [Ledder, Example 1.7.7.]

Goal and strategy:

- A population of microorganisms is distributed along a stream of length 10 with linear density $1000 e^{-0.1x}$ individuals per unit length.
- We aim at computing the the total number p of individuals in the stream.

Ingredients:

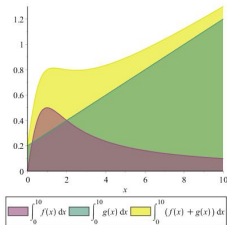
- The number of individuals associated in an infinitesimal portion of the stream $[x, x + dx]$ is $1000 e^{-0.1x} dx$.

Thus,

$$p = \int_0^{10} 1000 e^{-0.1x} dx.$$

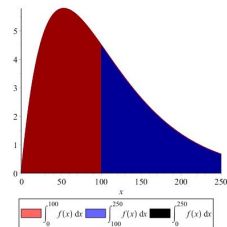
- **Linearity rule.** Let a , b , A , and B be any constants. If the functions f and g have integrals on the interval $[a, b]$, then

$$\int_a^b [Af(x) + Bg(x)] dx = A \int_a^b f(x) dx + B \int_a^b g(x) dx.$$



- **Partition rule.** If the function f has integrals on the intervals $[a, b]$ and $[b, c]$, then

$$\int_a^c f(x) dx = \int_a^b f(x) dx + \int_b^c f(x) dx.$$



We have the following important results.

Let $f : [a, b] \rightarrow \mathbb{R}$ be a bounded function.

- If f is monotone (increasing or decreasing), then it is Riemann integrable in $[a, b]$.
- If f is continuous, then it is Riemann integrable in $[a, b]$.
- If f is Riemann integrable in $[a, b]$, with $f([a, b]) \subset [c, d]$, and $g : [c, d] \rightarrow \mathbb{R}$ is continuous, then $g \circ f$ is Riemann integrable in $[a, b]$.

Warning! Not all bounded functions are Riemann integrable. For instance, the function $f : \mathbb{R} \rightarrow \mathbb{R}$ defined by

$$f(x) = \begin{cases} 1 & \text{if } x \notin \mathbb{Q} \\ 0 & \text{if } x \in \mathbb{Q} \end{cases},$$

is not Riemann integrable in any interval $[a, b]$.

- **Motivation.** $x(b) - x(a) = \int_a^b v(t) dt$ since $\Delta x \approx v(t) \Delta t$.
- **Statement (first “issue”).** Suppose F' is continuous on the interval $[a, b]$. Then,

$$\int_a^b F'(t) dt = F(b) - F(a).$$

In every accumulation problem, we express the total change in a quantity as the integral of the rate of change.

Example.

$$\int_0^\pi \sin x \, dx = -\cos \pi + \cos 0 = -(-1) + 1 = 2$$

taking $f(x) = -\cos x$ and so $f'(x) = \sin x$ as desired.

The fundamental theorem of calculus

Statement and sketch proof

Theorem. Let $f : [a, b] \rightarrow \mathbb{R}$ be a continuous function. Define $F : [a, b] \rightarrow \mathbb{R}$ as

$$F(x) = \int_a^x f(z) dz.$$

Then F is continuously differentiable, and $F' = f$.

Sketch of the proof. Notice that

$$F'(x) = \lim_{h \rightarrow 0} \frac{F(x+h) - F(x)}{h} = \lim_{h \rightarrow 0} \frac{1}{h} \int_x^{x+h} f(z) dz$$

and that, in $[x, x+h]$,

$$\int_x^{x+h} f(z) dz \simeq f(x)h.$$

The fundamental theorem of calculus

Barrow's rule

Definition: It is said that F , defined as $F(x) = \int_a^x f(z) dz$, is a *primitive* or *antiderivative* of f . A primitive of f is defined up to an additive constant. The set of all primitives of f is its *indefinite integral*, denoted by $\int f(x) dx$. Hence, we have:

$$\int f(x) dx = F(x) + C.$$

Corollary [Barrow's rule] Let $f : [a, b] \rightarrow \mathbb{R}$ be a continuous function, and $g : [a, b] \rightarrow \mathbb{R}$ a primitive of f . Then:

$$\int_a^b f(x) dx = [g(x)]_a^b := g(b) - g(a).$$

- **Table of elementary integrals (antiderivatives/primitives)** (just flipping the table of derivatives).

$f'(x)$	$x^r \ (r \neq -1)$	$\frac{1}{x}$	e^{ax}	$\cos ax$	$\sin ax$	$\frac{1}{a^2 + x^2}$	$\frac{1}{\sqrt{a^2 - x^2}}$
$f(x)$	$\frac{x^{r+1}}{r+1}$	$\log x $	$\frac{1}{a} e^{ax}$	$\frac{1}{a} \sin ax$	$-\frac{1}{a} \cos ax$	$\frac{1}{a} \arctan \frac{x}{a}$	$\arcsin \frac{x}{a}$

Example. $\int (x^2 + 1) dx = \frac{1}{3}x^3 + x + C$.

Exercise. Using a double-angle trigonometric formula, compute $\int 2 \sin x \cos x dx$.

Exercise. Check that $\int 2 \sin x \cos x dx = \sin^2 x + C$, but also $\int 2 \sin x \cos x dx = -\cos^2 x + C$. Why?

Exercise. The functions $\sinh x = \frac{1}{2}(e^x - e^{-x})$ and $\cosh x = \frac{1}{2}(e^x + e^{-x})$ are the *hyperbolic sine* and *cosine* functions. Compute their primitives.

■ Change of variables (substitution).

If f is differentiable and g is continuous with G as a primitive, then, by the chain rule, $G(f(x))$ is a primitive of $g(f(x))f'(x)$.

This is often written as

$$\int g(f(x))f'(x) dx = \int g(f(x)) df(x) = \int g(y)dy, \quad y = f(x),$$

and it is said that the change of variable $y = f(x)$ is performed.

■ Change of variables (substitution).

$$\int g(f(x))f'(x) dx = \int g(f(x)) df(x) = \int g(y)dy, \quad \text{where } y = f(x).$$

Example. $\int \sin(f(x))f'(x) dx = -\cos(f(x)) + C,$

$$\int \cos(f(x))f'(x) dx = \sin(f(x)) + C.$$

Example. $\int \frac{f'(x)}{f(x)} dx = \log |f(x)| + C.$

Example. $\int x\sqrt{2x^2+1} dx = \int \frac{\sqrt{y}}{4} dy$, with $y = 2x^2 + 1$. Then,

$$\int x\sqrt{2x^2+1} dx = \frac{1}{6}y^{3/2} + C = \frac{1}{6}(2x^2+1)^{3/2} + C.$$

Exercise. Compute: (a) $\int x \sin(x^2) dx$; (b) $\int \frac{\log x}{x} dx$.

■ Integration by parts.

If F, G are two primitives of f, g respectively, then, by Leibniz rule of the derivative of the product, $(FG)' = fG + Fg$, so that $Fg = (FG)' - fG$. Then,

$$\int F(x)g(x) dx = F(x)G(x) - \int f(x)G(x) dx.$$

A usual way of writing the formula is

$$\int u dv = uv - \int v du, \quad \text{where } du = u' dx, dv = v' dx.$$

Example. $\int x \sin x dx = -x \cos x + \int \cos x dx = -x \cos x + \sin x + C.$

Example. $\int \log x dx = \int 1 \cdot \log x dx = x \log x - \int x \frac{1}{x} dx = x \log x - x + C.$

Example. $\int x^2 e^x dx = x^2 e^x - \int 2x e^x dx = x^2 e^x - (2x e^x - \int 2e^x dx) = x^2 e^x - 2x e^x + 2e^x + C = (x^2 - 2x + 2)e^x.$

Exercise. Write an algorithm to compute $\int p(x)e^x dx$, where $p(x)$ is a polynomial.

Exercise. Compute $\int e^x \sin x dx$ by integrating by parts two times.

The art of computing primitives is based on the previous two methods. The idea is simply get a suitable change of variable or performing integration by parts, so that the following integral is simpler and reduced to one we can solve. With these methods, one can compute **explicitly** the primitives of the following functions:

- $p(x)e^{ax}$, $p(x)\sin(ax)$, $p(x)\cos(ax)$, $p(x)\log(x)$, $p(x)\arctan(x)$ ($p(x)$ is a polynomial);
- $e^{ax}\sin(bx)$, $e^{ax}\cos(bx)$;
- rational functions $\frac{p(x)}{q(x)}$, where $p(x)$, $q(x)$ are polynomials;
- trigonometric rational functions $R(\sin x, \cos x)$, where $R(s, c)$ is a rational function in the variables s, c ;
- (some) irrational functions;
- functions with square roots of polynomials.

There are implementations of these methodologies, based on symbolic calculus.

Unfortunately, **there are much more functions for which one can not obtain an explicit formula** for the primitive. Some simple examples are the apparently naive functions e^{-x^2} , $\sin x^2$ or $\frac{1}{x} \sin x$.

Problem: We want to compute

$$\int_0^1 \frac{\sin x}{x} dx,$$

but, unfortunately, the primitive of $f(x) = \frac{\sin x}{x}$ can not be expressed by means of elementary functions.

Solution: By integrating at interval $[0, x]$ the power series of $f(x)$, we obtain:

$$\int_0^x \frac{\sin x}{x} dx = \sum_{n=0}^{\infty} \frac{(-1)^n x^{2n+1}}{(2n+1)(2n+1)!}.$$

In particular,

$$\int_0^1 \frac{\sin x}{x} dx = \sum_{n=0}^{\infty} \frac{(-1)^n}{(2n+1)(2n+1)!}.$$

Problem: We aim at computing the integral of a function f in an interval $[a, b]$. . . but several restrictions may arise:

- we have the expression of f , but we are not able to explicitly compute a primitive; or,
- we do not have the expression of f , but we have a recipe to evaluate it; or
- we have a table of values of f (most likely, coming from experimental data).

Then, we can approximate the integral by means of some numerical integration formula.

Problem: The function

$$f(x) = \frac{1}{\sqrt{2\pi}} e^{-\frac{1}{2}x^2},$$

is known as *normal density function with mean $\mu = 0$ and standard deviation $\sigma = 1$* .

The probability that a value randomly chosen according to this probability distribution belongs to the interval $[a, b]$ is given by $\int_a^b f(x) dx$. It is **not possible to express this integral as a composition of "elementary" functions**.

Question: How can we **approximate, with accuracy** of 10^{-5} , that a value randomly chosen according to this probability distribution belongs to the interval $[-2, 2]$?

Problem: Numerical computation of the integral defined by a function f in an interval $[a, b]$,

$$I(f) = \int_a^b f(x) dx, \approx \sum_{i=1}^n c_i f(x_i) \text{ for some } c_i \in \mathbb{R}$$

either from the mathematical expression of f or from a table of values of f .

Basic ideas:

- Approximate f by a polynomial p , and take

$$I(f) \approx \int_a^b p(x) dx .$$

(simple numerical integration formulas).

- Divide the interval $[a, b]$ in subintervals, and use the simple numerical integration formulas in each of the subintervals.
(composite numerical integration formulas).

In order to estimate the value of $I(f)$ from the values of f at points a , b and $c = \frac{1}{2}(a + b)$, we can use:

- **Rectangle rule:** Approximating f by the constant $f(c)$ we get

$$I(f) \approx I_R(f) = (b - a)f(c) .$$

- **Trapezoid rule:** Approximating f by the straight line through $(a, f(a))$ and $(b, f(b))$, we get

$$I(f) \approx I_T(f) = \frac{(b - a)}{2}(f(a) + f(b)) .$$

- **Simpson's formula:** Approximating f by the parabola through the points $(a, f(a))$, $(c, f(c))$ and $(b, f(b))$, we get

$$I(f) \approx I_S(f) = \frac{b - a}{6}(f(a) + 4f(c) + f(b)) = \frac{c - a}{3}(f(a) + 4f(c) + f(b)) .$$

Dividing the interval $[a, b]$ in subintervals, we can apply the simple formulas in each of them: we choose the nodes $\{x_i = a + ih\}_{i=0}^n$, on $h = \frac{b-a}{n}$.

- **Composite rectangle rule.** If $y_i = \frac{1}{2}(x_{i-1} + x_i)$:

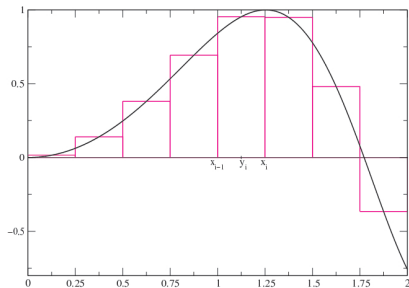
$$I_R(f, h) = h(f(y_1) + f(y_2) + f(y_3) + \cdots + f(y_{n-1}) + f(y_n)).$$

- **Composite trapezoid rule:**

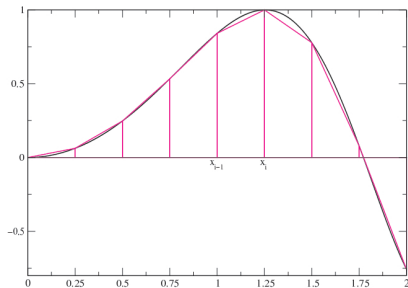
$$I_T(f, h) = \frac{h}{2}(f(x_0) + 2f(x_1) + 2f(x_2) + \cdots + 2f(x_{n-1}) + f(x_n)).$$

- **Composite Simpson's formula.** If n is even, we can apply Simpson's rule to the intervals $[x_0, x_2]$, $[x_2, x_4]$, ..., $[x_{n-2}, x_n]$:

$$I_S(f, h) = \frac{h}{3}(f(x_0) + 4f(x_1) + 2f(x_2) + 4f(x_3) + \cdots + 2f(x_{n-2}) + 4f(x_{n-1}) + f(x_n)).$$



Approximation by rectangles



Approximation by trapezoids

Example: Computation of $\int_0^2 \sin(x^2) dx$

n	Rectangles	Trapezoids	Simpson
2	1.025477156142	0.463069737154	0.869693814641
4	0.837368896902	0.744273446648	0.838008016480
8	0.811881955543	0.790821171775	0.806337080151
16	0.806496669270	0.801351563659	0.804861694287
32	0.805203153963	0.803924116465	0.804781634067
64	0.804882946231	0.804563635214	0.804776808130
128	0.804803090517	0.804723290722	0.804776509225
256	0.804783138822	0.804763190620	0.804776490586
512	0.804778151662	0.804773164721	0.804776489421
1024	0.804776904920	0.804775658192	0.804776489349
2048	0.804776593238	0.804776281556	0.804776489344
4096	0.804776515317	0.804776437397	0.804776489344
8192	0.804776495837	0.804776476357	0.804776489344
16384	0.804776490967	0.804776486097	0.804776489344

Exact value: 0.8047764893437561 ...

R) $l(f) = l_R(f, h) + \frac{(b-a)}{24} f^{(2)}(\xi) h^2 = l_R(f, h) + O(h^2)$ and an error bound is $E_R(f, h) = \frac{(b-a)^3}{24 n^2} M_2$;

T) $l(f) = l_T(f, h) - \frac{(b-a)}{12} f^{(2)}(\xi) h^2 = l_T(f, h) + O(h^2)$ and an error bound is $E_T(f, h) = \frac{(b-a)^3}{12 n^2} M_2$;

S) $l(f) = l_S(f, h) - \frac{(b-a)}{180} f^{(4)}(\xi) h^4 = l_S(f, h) + O(h^4)$ and an error bound is $E_S(f, h) = \frac{(b-a)^5}{180 n^4} M_4$;

where

- h is the distance between nodes, that is $h = \frac{b-a}{n}$;
- M_2 and M_4 are bounds of $|f^{(2)}(x)|$ and $|f^{(4)}(x)|$ in $[a, b]$.

Problem: How many intervals do we need to compute

$$\int_0^2 \sin(x^2) dx$$

with an error less than $\varepsilon = 10^{-6}$, using R,T,S?

Solution: Approximated bounds for the second and fourth derivatives of $f(x) = \sin(x^2)$ (in absolute value) are $M_2 = 11$ and $M_4 = 165$, respectively. Then:

- For R, $n \geq \left(\frac{(b-a)^3 M_2}{24\varepsilon} \right)^{\frac{1}{2}} = 1914.85$ and $n = 1915$;
- For T, $n \geq \left(\frac{(b-a)^3 M_2}{12\varepsilon} \right)^{\frac{1}{2}} = 2708.01$ and $n = 2709$;
- For S, $n \geq \left(\frac{(b-a)^5 M_4}{180\varepsilon} \right)^{\frac{1}{4}} = 73.60$ and $n = 74$ (recall that Simpson's formula requires n to be even).

Solution to the initial problem:

We would like to compute

$$P := \frac{1}{\sqrt{2\pi}} \int_{-2}^2 e^{-\frac{1}{2}x^2} dt$$

Let $g(x) = e^{-\frac{1}{2}x^2}$. We have that $M_2 = 1$ and $M_4 = 3$.

- Rectangles: $n = 517$
- Trapezoids: $n = 731$
- Simpson: $n = 38$

Using composite Simpson's rule, we obtain

$$P \approx \frac{1}{\sqrt{2\pi}} 2.392576 \approx 0.9545.$$

Differential equations

Definitions and examples

In general, a **ordinary differential equation (ODE)** associated to an evolutionary process $y(t)$ is an equation that relates the rates of change of the states with the states themselves.

$$\mathcal{F}(t, y(t), y'(t), \dots, y^{(n)}(t)) = 0$$

The highest order of derivation that appears in a differential equation is called **the order** of the differential equation.

- $\dot{y}(t) = -\kappa y(t)$ has order 1; in general, $\dot{x}(t) = f(x(t))$ has order 1.
- $\frac{dx}{dt} = r x - \frac{q x}{a + x}$, $a, q, r > 0$, has order 1.
- $x''(t) = a$ ($a \in \mathbb{R}$) has order 2.
- $x''(t) + f(x(t)) x'(t) + g(x(t)) = 0$ (f, g continuous functions) has order 2.

- Sometimes, we avoid writing the independent variable (it is implicitly assumed to be there and can be deduced from the context):

- $\dot{y} = -\kappa y$, $\dot{x} = r x - q x / (a + x)$, $x'' = a$, $x'' + f(x) x' + g(x) = 0, \dots$

Note also that the derivative is expressed with different notations:

$$\frac{dx}{dt} = x'(t) = \dot{x}(t) = \dots$$

- When the evolutionary process depends on more than one variable, the differential equation is called a **partial differential equation**. For instance

$$\frac{\partial^2 u}{\partial t^2} = \alpha \frac{\partial^2 u}{\partial x^2},$$

where $u = u(t, x)$ is the temperature at time t on the position x along a 1D axis (it is called the *heat equation*).

We have seen different **examples of ordinary differential equations** along the course that we revisit here in short.

The **rate of change of the amount of drug** and the **amount** itself are related by

$$\dot{y}(t) = -\kappa y(t).$$

This is the law of the decay of the drug, a **differential equation** that encodes all possible evolutions of the system.

Assume Ibuprofen is **slowly absorbed** from the digestive system and **relatively quickly eliminated** from the body.

Let be:

- x , the amount of **drug in the digestive system**;
- y , the amount of **drug in the bloodstream**.

Notice that, initially, the whole dose A is in the digestive system, thus $x(0) = A$, $y(0) = 0$. We get the **system** of ODEs:

$$\begin{cases} \dot{x}(t) &= -b x(t), \\ \dot{y}(t) &= -k y(t) + b x(t), \end{cases}$$

where k is the clearance rate for the bloodstream, and b is the clearance rate for the digestive system.

$$x(t) = Ae^{-bt}, \quad y(t) = \frac{Ab}{b-k} (e^{-kt} - e^{-bt})$$

Population dynamics is the branch of life sciences that studies the **size and age composition of populations** as dynamic systems, **and the biological and environmental processes driving them** (such as birth and death rates, migrations, ...). Simple models for the **size x** of a biological population are:

- *Malthus' model*, or equation of normal reproduction (like bacteria in a Petri dish):

$$\dot{x} = rx, \quad r > 0.$$

The rate of reproduction (or *birth rate*) is proportional (with constant r) to the number of organisms present.

- *Verhulst's model*, or *logistic equation*:

$$\dot{x} = rx(1 - x/K), \quad r > 0, K > 0.$$

The competition for food leads to a decrease of the birth rate which depends on the size of the population; K is called the *carrying capacity*.

- Logistic growth with **emigration**:

$$\dot{x} = r x (1 - x/K) - c, \quad r > 0, K > 0, c > 0, \quad (1)$$

where c models the rate of emigration. In fact, the model does not only model emigration but also other subtracting effects like **harvesting**, **hunting**, **fishing**, **herbivory**,...

- Adding general **consumption rates**, we get:

$$\frac{dx}{dt} = r x - \frac{q x}{a + x}, \quad a, q, r > 0,$$

In Problem 2.12, the first term represented plant growth and the second represented herbivory.

Solving differential equations: quantitative and qualitative methods

The evolution of the system is (presumably) determined by the initial condition, say $y(0) = A$. We have then to solve an **initial value problem**¹:

$$\dot{y}(t) = -\kappa y(t), \quad y(0) = A.$$

Notice that $y(t) > 0$, so that we can divide by $y(t)$ to get

$$-\kappa = \frac{\dot{y}(t)}{y(t)} = \frac{d}{dt}(\log y(t)).$$

Integrating from time 0 to t both sides of the equation, we get:

$$-\kappa t = \int_0^t \frac{d}{dt}(\log y(t)) dt = [\log y(t)]_0^t = \log y(t) - \log A = \log \left(\frac{y(t)}{A} \right),$$

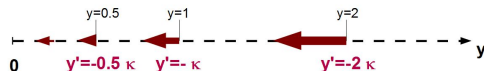
where we have used the fundamental theorem of calculus, aka Barrow's rule. Finally, we get the expected evolution

$$y(t) = e^{-\kappa t} A.$$

¹General solution, particular solution.

Remarks:

- Observe that we need to integrate to solve a differential equations. In particular ODEs of type $y'(x) = f(x)$ are equivalent to solving $\int f(x) dx$. Differential equation/initial value problem are related, respectively, to indefinite/definite integral;
- Most of the differential equations can not be solved by hand, and one can use numerical methods (also known as **integration methods**, as in Lecture 06), whose theoretical basis are, generally, Taylor expansion and interpolation.
- Global features of the systems can be studied by using **qualitative rather than quantitative approach**. In the present example:

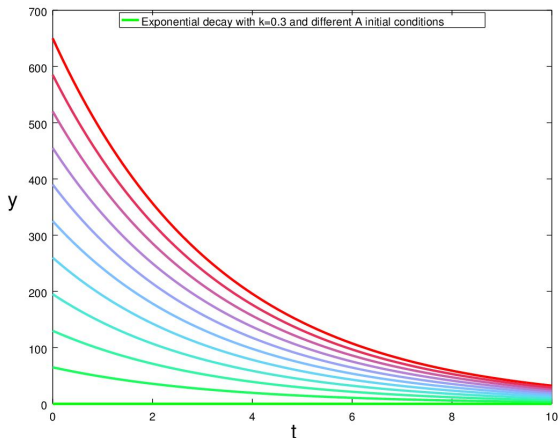
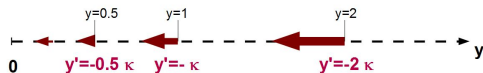


Modeling drug clearance

Solving a simple differential equation

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$$\dot{y}(t) = -\kappa y(t), \quad y(0) = A;$$

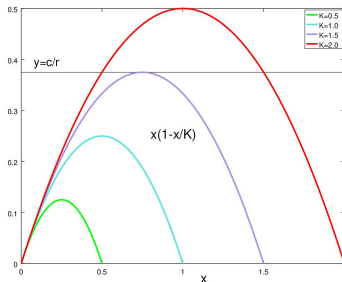


$$\dot{x} = r x (1 - x/K) - c =: f(x; r, K, c), \quad r > 0, K > 0, c > 0.$$

- We study the **sign of $\dot{x}$** . Accordingly, we solve

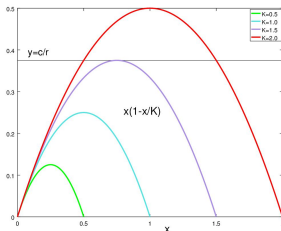
$$f(x; r, K, c) = 0 \Rightarrow x(1 - x/K) = c/r,$$

which are called **equilibria**.



Obs.: $f = 0$ at $x = 0, K$, $f > 0$ iff $x \in (0, K)$, $f' = 0$ at $x = K/2$, $f(K/2) = K/4$ and $f'(0; r, K, c) = r$.

$$\dot{x} = r x (1 - x/K) - c =: f(x; r, K, c), \quad r > 0, K > 0, c > 0.$$



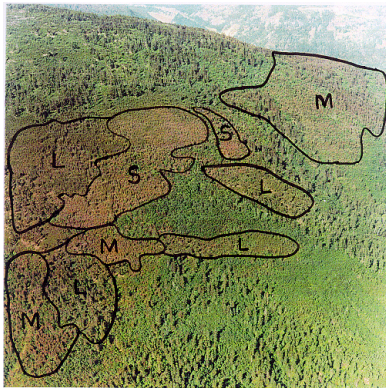
$$f = 0 \text{ at } x = 0, K; f > 0 \text{ iff } x \in (0, K); f' = 0 \text{ at } x = K/2, f(K/2) = K/4; f'(0; r, K, c) = r.$$

- The equation can have 0, 1 or 2 equilibria. There is a **(saddle-node bifurcation)** when $c = (rK)/4$ (computations on the blackboard).
- When $c < (rK)/4$, $x_{\pm}^* := \frac{K}{2r} \left(r \pm \sqrt{r^2 - 4cr/K} \right)$ are the equilibria; x_-^* **unstable** and x_+^* is **stable** (hint: look at the sign of $f(x)$).
- When $c = (rK)/4$, $x^* := x_-^* = x_+^* = \frac{K}{2}$ is the unique equilibrium and is **semistable**.

Remark: **Bifurcation analysis** let us study the different possible behaviours of a system with respect to certain control parameters (like r , K , c), so we can tune them appropriately to get a desired effect.

Exercise: Prove that $f'(x_-^*) > 0$ and $f'(x_+^*) < 0$ when $c < (rK)/4$, and $f'(x^*) = 0$, $f''(x^*) < 0$ when $c = (rK)/4$. Observe that, in general, the sign of f' at the equilibrium points determines their stability character. Find and classify the equilibrium points of $\dot{x} = f(x)$ when $f(x) = x^2$ and $f(x) = x^3$.

Spruce budworm (*Choristoneura fumiferana*) damage appears in May. Evidence of a spruce budworm infestation includes the destruction of buds, abnormal spreading of new twigs, defoliation of current-year shoots and, if an affected branch is disturbed, the presence of large numbers of larvae suspended from strands of silk.



Pest damage: Examples of LIGHT, MODERATE and SEVERE mortality of lodgepole pine. See also http://www.ncrs.fs.fed.us/gla/natdist/mn_sbw.htm

A model for Spruce Budworm

Qualitative analysis and bifurcation analysis for the logistic growth with general rate of consumption

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$$\dot{x} = r x (1 - x/K) - \frac{x^2}{1 + x^2}, \quad r > 0, K > 0, q > 0.$$

- $x = 0$ is always an **unstable** equilibrium.
- Depending on the parameter values, we can have 0, 1 or 2 more equilibria. All is reduced to study the intersections between functions $g(x) := r(1 - x/K)$ and $h(x) := x/(1 + x^2)$ (see figures below and computations on the blackboard).

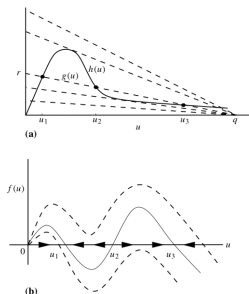


Figure 1.5. Equilibrium states for the spruce budworm population model (1.8). The positive equilibria are given by the intersections of the straight line $r(1 - u/q)$ and $u/(1 + u^2)$. With the middle straight line in (a) there are 3 steady states with $f(u; r, q)$ typically as in (b).

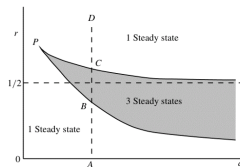
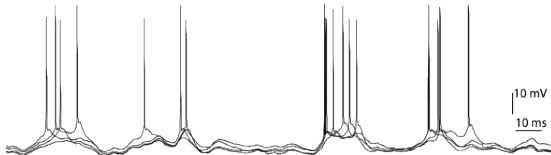
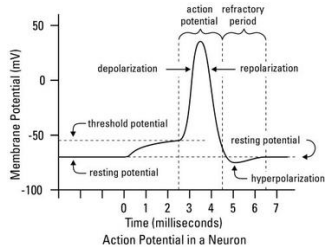
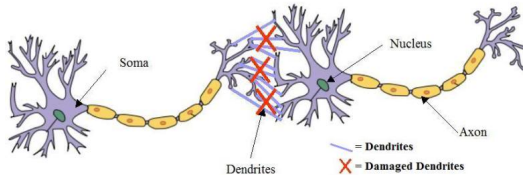


Figure 1.6. Parameter domain for the number of positive steady states for the budworm model (1.8). The boundary curves are given parametrically (see Exercise 1) by $r(a) = 2a^3/(a^2 + 1)^2$, $q(a) = 2a^3/(a^2 - 1)$ for $a \geq \sqrt{3}$, the value giving the cusp point P .

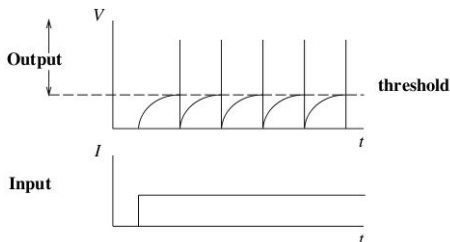
Intersections giving equilibria and
2-parameter bifurcation diagram ($q = K$
in our example).



$$C \frac{dv}{dt} = -g_L (v - V_L) + I(t),$$

- **Spike detection:** if $v(t) > V_{thresh}$, then we compute a spike and $v(t + T_{ref}) = V_{reset}$ (resetting).

Notation: $v = v(t)$ is the membrane potential $V_{in} - V_{out}$, C is the membrane capacitance, g_L is the leakage conductance, V_L is the leakage reversal potential, V_{reset} is a reset voltage (close to the lowest possible), V_{thresh} is a threshold voltage where a spike is initiated and T_{ref} is a refractory time related to the spike duration ($C > 0$, $g_L > 0$, V_L , V_{reset} , V_{thresh} , $T_{ref} \geq 0$ are assumed to be known and fixed here). $I(t)$ is the injected current.



Simulation of a neuron's membrane potential using an I&F model with $T_{ref} > 0$

The equation

$$C \frac{dv}{dt} = -g_L (v - V_L) + I(t),$$

is a **linear differential equation**. We will solve it both quantitatively (LDE can be always solved) and qualitatively. We take $C = 1$ for simplicity).

Case $I(t) = I$ constant:

- $v = V_L + I/g_L$ is a stable fixed point. Then, we will have spikes if and only if $V_{thresh} < V_L + I/g_L$.
- For $I = 0$, $v(t) = V_L + (v_0 - V_L) \exp(-g_L (t - t_0))$, assuming $v(t_0) = v_0$ (initial value problem). Hint: use $z(t) := v(t) - V_L$. Observe that

$$\lim_{t \rightarrow +\infty} v(t) = V_L.$$

- For $I \neq 0$, we assume $z(t) = C(t) \exp(-g_L (t - t_0))$ and we get (after computations):

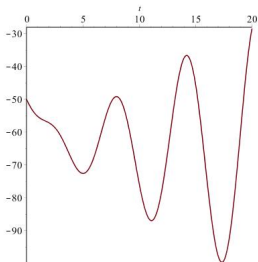
$$v(t) - V_L = I/g_L + (v_0 - V_L - I/g_L) \exp(-g_L (t - t_0)); \text{ thus, } \lim_{t \rightarrow +\infty} v(t) = V_L + I/g_L.$$

$$C \frac{dv}{dt} = -g_L (v - V_L) + I(t).$$

Case $I(t)$ variable (non-autonomous LDE):

Solving by variation of constants:

$$v(t) - V_L = (v_0 - V_L) \exp(-g_L (t - t_0)) + \int_{t_0}^t I(s) \exp(-g_L (t - s)) ds.$$



Simulation of $v(t)$ using $V_L = -65$ mV,
 $gL = 0.5$ mS/cm², $v_0 = -50$ mV, $t_0 = 0$ ms and
 $I(t) = t \sin(t) \mu$ A/cm².