MATRIC MODELING SEMINAR August 9, 2016

Integrating mathematics and modelling into life science programs

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Contents

1. What is the context?

- Insufficient basic mathematics skills of many first-year life science students
- Heterogeneous intake (Math A/B, NG/NT)
- Limited time for brushing up competencies
- Demands at UvA Life Sciences:
  Learning mathematics in context,
  e.g. *mathematical models of growth,*
  Hodgkin-Huxley neural model
- Work in progress: *finding the right balance between pure mathematics and modelling*

Description of cohort 2015-2016

- 500 freshmen:

  ±250 : Biology, biomedical sciences

  ±250 : Psychobiology; in March ±160 remaining (Binding Study Advice)

- Basic mathematics in the bachelors programs

  Biology & Biomedical sciences

  ICT Mathematics in block 1 (8 weeks), part of *From Molecule to Cell*

  Psychobiology

  Basic Mathematics (lectures + tutorials + SOWISO) in block 4 and 5 (10 weeks), stand-alone 3 EC course

  Digital exam

Description of cohort 2015-2016

	total	**psycho-biology**	**biomedical sciences**	**biology**
number of students	500	250 (156 in March)	186	67
gender male / female		33 / 118	72 / 113	41 / 26
vwo-math A / B		**46** / 107	49 / 119	26 / 38
profile NG / NT		82 / 69	110 / 63	41 / 23
mean mark vwo-math (SD)		7.1 (1.0)	6.9 (1.0)	6.5 (0.7)
mean mark entry test (SD)		7.3 (1.5)	6.8 (1.6)	6.9 (1.7)

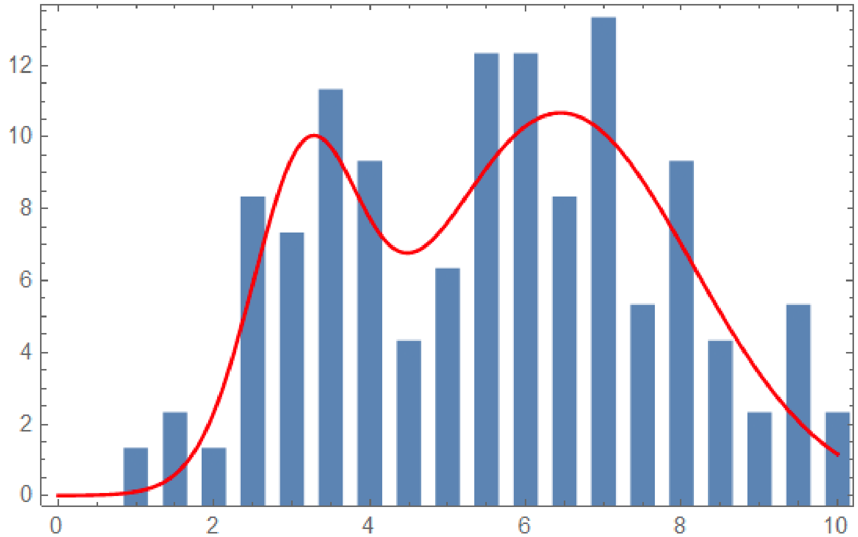
Digital exam

Exam results psychobiology 2016

- Exam results of freshmen

	pass	no pass	total
Math A	5 (19%)	21 (81%)	26 (22%)
Math B	56 (69%)	25 (31%)	81 (69%)
Math B & D	9 (90%)	1 (10%)	10 (9%)
total	70 (60%)	47 (40%)	117 (100%)

- Histogram of score



Some disappointing results

- Solve $\tan(x) = \sqrt{3}$ in the interval $\left(-\frac{\pi}{2}, \frac{\pi}{2}\right)$

  p-value 0.41 (calculator addiction)

- For what real numbers *p* does the graph of $f(x) = px^2 + 2x + 1$ not intersect the *x*-axis?

  p-value 0.39 (difficulties in working with parameters)

- How can $\sqrt{(x^2 - 1)^2 + 4x^2}$ be simplified? (resit ’15)

  (a) $x^2 + 2x - 1$ (b) $x^2 + 1$

  (c) $3x^2 + 1$ (d) $2x^2 - 2x$

  p-value 0.11 (little symbol sense)

Requested course contents

- Biomedical Sciences & Biology:
  - Chemical calculations (molarity, pH, dilution)
  - Basic calculus (functions (no goniometric functions), differentiation)
  - Models of growth (exponential & limited growth models)

- Psychobiology
  - Calculus: functions (incl. gonio functions), differentiation, integration
  - Complex numbers
  - Basic linear algebra: matrix algebra, eigenvalues & eigenvectors
  - Differential equations: basic methods, Euler's solution method

How realistic in a short 3EC course? What about modelling?

Unrealistic expections

“What I noticed is that you do not mention the solution method for the logistic differential equation. I think it is useful, should perhaps be worked out, and linked to Wikipedia where students can find it!”

By ***separation of variables***

thus $$\frac{dN}{dt} = kN(M-N),$$

$$\frac{dN}{N(M-N)} = k\,dt\,,$$

and by ***integration*** and ***partial fraction decomposition***

$$\int k\,dt + C = \int \frac{1}{N(M-N)}dN = \frac{1}{M}\int \left(\frac{1}{N} + \frac{1}{M-N}\right) dN,$$

and $$kMt + C' = \log|N| - \log|M-N| = \log\left|\frac{N}{M-N}\right|$$

Many points of view

Comment from 3rd year lecturer in neuroscience

“I agree that it is necessary for students interested in computational topics to have a stronger mathematical background. Indeed algebra is necessary. I also strongly believe that an actual "Calculus" course would be better than a "basic math" course. It might seem less applied at first, but it would give them a strongest background. The same - in my opinion - should be done for Physics (and Chemistry), as without theoretical background it will be hard for them to make proper models.”

Design computational neuroscience

- For all students:
  - Basic computational skills (numeric and algebraic)
  - Mathematical functions: (properties of linear functins, powers, polynomials, exponential functios and logarithm, goniometric functions)
  - Differentiation and derivatives
  - Differentials and integration
  - Complex numbers,
  - Introduction to differential equations

In short, my current basic mathematic course!

Models and modelling included (at small scale)

Design computational neuroscience

- For students in computational track:
  - Advanced calculus (Taylor series, limits, …)
  - Dynamical systems (phase portrait, equilibria, stability analysis)
  - Signal analysis: (Fourier analysis, filtering, convolution)
  - Neural modelling (rate model, integrate-and fire model)
  - Linear algebra (matrix algebra, linear equations, eigenvalues)

- Find a good balance: not too much, nor too few math

- Let students develop a '*quantitative attitude*'

  Let students learn to search for quantitative solutions to neuroscience problems (simulations included), and not to be afraid of searching for quantitative relations in raw data.

2. What form of e-learning of basic mathematics in life sciences?

- Digital context rich modules with theory, randomised examples and exercises
- Blended approach: Lectures + tutorials + digital exercising and home study + formative assessments
- Mixture of context problems and pure mathematics exercises
- Goal setting: score ≥ 8.0 required for each digital assessment
- Digital feedback for student, tutor and teacher
- Support via forum and email

Implementation

- via SOWISO environment for learning, doing and assessing mathematics (www.sowiso.nl)

- tour in SOWISO

  Some screen shots follow

Have a look yourself at uva.sowiso.nl/auth/login

with account matric1 and password andreheck

A worked-out solution

molarity calculation

How many grams of sulfuric acid (H_2SO_4) are contained in $300\ \mathrm{mL}$ of a sulfuric acid solution with sulfate ion concentration (SO_4^{2-}) of $0.60\ \mathrm{mol/L}$?
Round the numeric answer to one decimal place.

The atomic mass of hydrogen (H), sulfur (S), and oxygen (O) are:
$M(\mathrm{H}) = 1.008\ \mathrm{u}$, $M(\mathrm{S}) = 32.064\ \mathrm{u}$ and $M(\mathrm{O}) = 15.999\ \mathrm{u}$.

When the sulfate ion concentration is equal to $0.60\ \mathrm{mol/L}$, one also has a $0.60\ \mathrm{M}$ sulfuric acid solution. This means that there is $0.60\ \mathrm{mol}$ sulfuric acid (H_2SO_4) per liter liter of solution. Thus, $300\ \mathrm{mL}$ of the solution contains $300 \times \frac{1}{1000} \times 0.60 = 0.18\ \mathrm{mol}$ sulfuric acid.
The molar mass of sulfuric acid can be computed from the given atomic masses:

$$M(\mathrm{H_2SO_4}) = 2 \times M(\mathrm{H}) + M(\mathrm{S}) + 4 \times M(\mathrm{O}) = 98.076\ \mathrm{g/mol}.$$

$0.18\ \mathrm{mol}$ sulfuric acid corresponds with $0.18 \times 98.076 = 17.654\ \mathrm{gram}$ sulfuric acid (rounded to three decimal places). After rounding this intermediate result to one decimal, we conclude that $300\ \mathrm{mL}$ of a $0.60\ \mathrm{M}$ sulfuric acid solution contains $17.7\ \mathrm{gram}$ sulfuric acid.

Stepwise practice

Applying the substitution rule

Compute:

$$\int (5y+3)^4\,dy$$

Hint
Use the substitution rule

$$\int (5y+3)^4\,dy = \quad \_\_$$

Check

step-by-step

Applying the substitution rule: a.

Apply the substitution $u = 5y + 3$ to the following integral

$$\int (5y+3)^4 \, dy$$

What integral in u do you get then?

$$\int \_\_ \quad du$$

Check

Solution

Applying the substitution rule: a.

Apply the substitution $u = 5y + 3$ to the following integral

$$\int (5y+3)^4 \, dy$$

What integral in u do you get then?

$\int u^4 \, du$ — Wrong.Don't forget to compute the correct factor in front of the power.

$\int \frac{1}{5} u^4 \, du$ — Correct answer

continue › ✖ stop ? ask question

Applying the substitution rule: b.

After the substituion $u = 5y + 3$ the integral $\int (5y+3)^4\, dy$ gets replaced by the simpler integral

$$\int \frac{1}{5}\, u^4\, du$$

Compute this integral

$$\int \frac{1}{5}\, u^4\, du = \quad \_\_\_$$

Check

Solution

Applying the substitution rule: b.

After the substituion $u = 5y + 3$ the integral $\int (5y+3)^4\, dy$ gets replaced by the simpler integral

$$\int \frac{1}{5} u^4\, du$$

Compute this integral

$$\int \frac{1}{5} u^4\, du = \frac{1}{5} u^5$$

Don't forget to compute the correct factor in front of the power.

$$\int \frac{1}{5} u^4\, du = \frac{1}{25} u^5$$

Don't forget the constant of integration.

$$\int \frac{1}{5} u^4\, du = 0.04u^5 + c$$

Correct

Applying the substitution rule: c.

We have turned the integration

$$\int (5y+3)^4\, dy$$

via the substitution $u = 5y+3$ into the integration problem

$$\int \frac{1}{5}\, u^4$$

the solution of which is

$$\frac{1}{25}\, u^5 + c$$

.

Wat does this mean for the original integration problem

$$\int (5y+3)^4\, dy = \frac{1}{25}\,(5y+3)^5 + c$$

✓ Fine

Screen as worksheet

Simplify the expression $\frac{4e^{7x}}{2e^{5x}}$ into the form $b \cdot e^{c \cdot x}$.

$\frac{4e^{7x}}{2e^{5x}} = 2 \cdot \frac{\mathrm{e}^{7x}}{\mathrm{e}^{5x}}$ Not yet in the requested form.
Did you simply copy the expression from the question or is a fraction still remaining?

$\frac{4e^{7x}}{2e^{5x}} = 2 \cdot \mathrm{e}^{7x} \cdot \mathrm{e}^{-5x}$ Simplify further

$\frac{4e^{7x}}{2e^{5x}} = 2 \cdot \mathrm{e}^{7x-5x}$ OK, but not yet in the requested form

$\frac{4e^{7x}}{2e^{5x}} = 2 \cdot \mathrm{e}^{2x}$ Okay

PDF of course notes and assessments

Question 3

What is the number of significant digits in 6.00×10^{-8}?

a. 1
b. 2
c. 3
d. 5

Theory: Computational rules: multiplication and division

When you compute with floating-point numbers you must write the outcome with the right number of significant digits and, if necessary, round off to this number of digits. The below example illustrates this.

Example

A square room has the following dimensions: 2.5×3.5 m. **What** is the area?
It holds: $2.5 \times 4.5 = 11.25$, but in this notation there are more siginificant digits than in any factor. The accuracy cannot increase by a computation and therefore we round off to 2 significant digits, in this case 11.
Thus, the requested area is equal to 11. m^2.

You can also interpret the above computational outcome as follows:

Because the measured size of the room is given by numbers with a precision of 1 decimal, the dimensions of the room are at a minimum of 2.4×4.4 m at a maximum of 2.6×4.6 m. Thus, the area is between $2.4 \times 4.4 = 10.56$ and $2.6 \times 4.6 = 11.96$. Taking notice of these outcomes it seems fait to round off to two significant digits.

During computations you must not round off in intermediate steps. Instead you must compute with some extra significant digits (often 1 extra) until you arive at the final result and then round off using the following general rule:

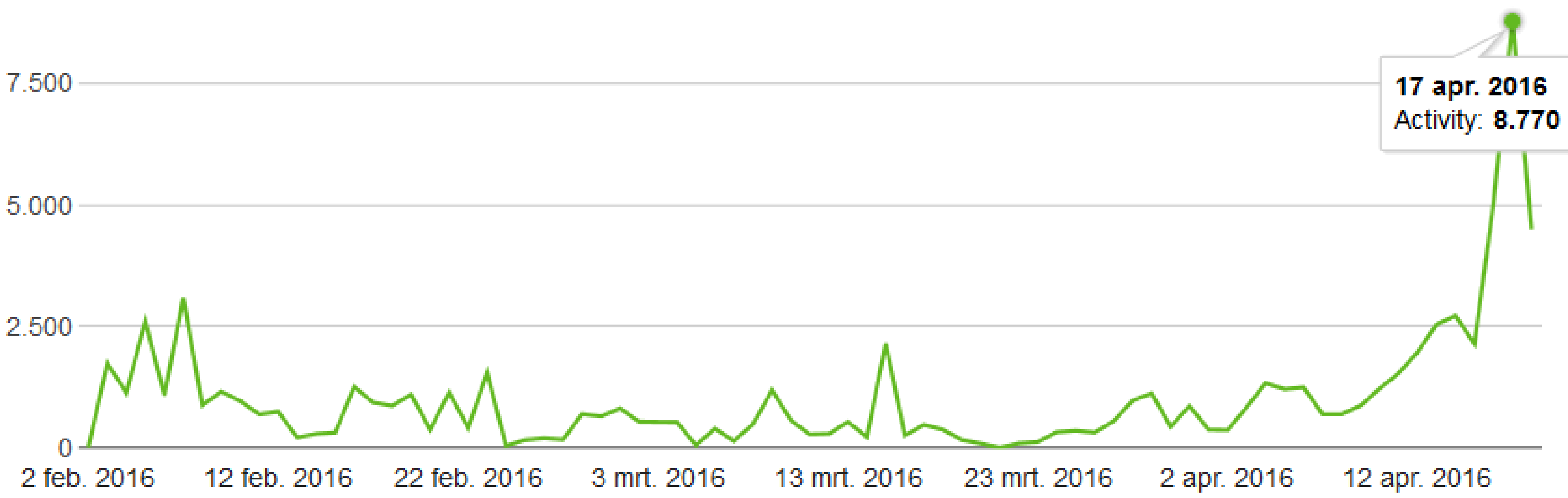
Statement

For multiplication and division holds:
The outcome of a computation has the same number of significant digits as the given quantity with the least number of significant digits.

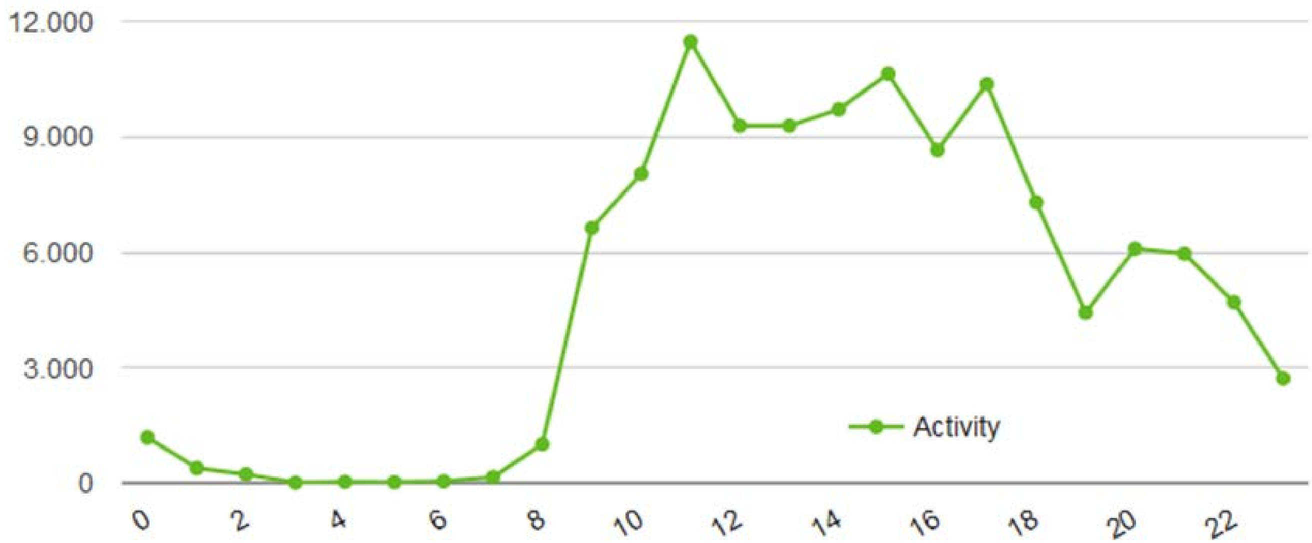
Participation in 2016

In 10 weeks, by 228 students:

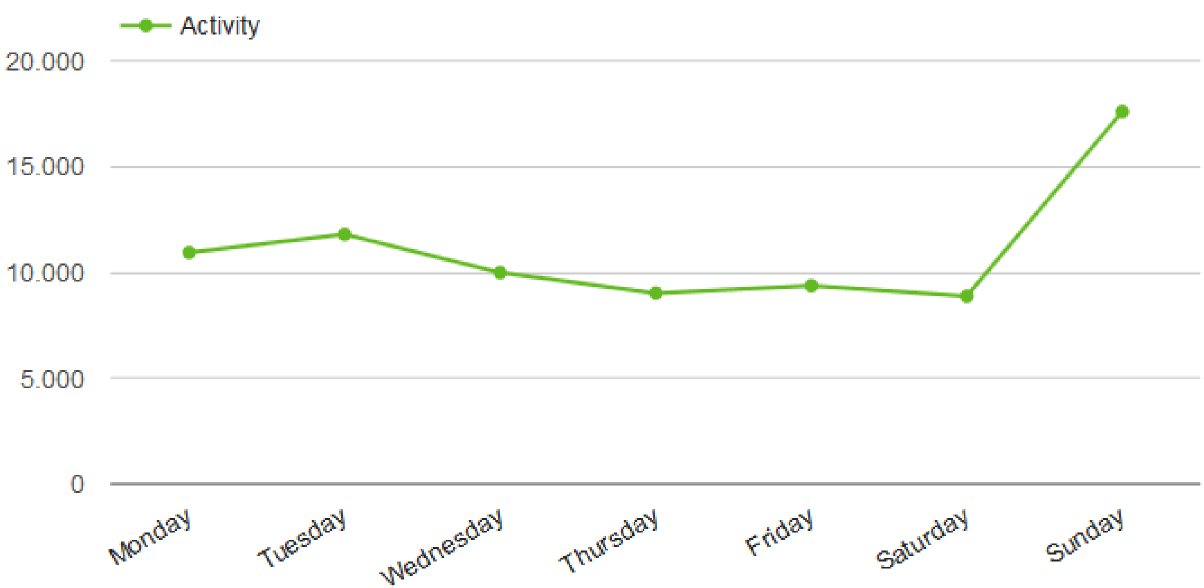
- 37,196 exercises made (outside assessments)
- average of 163 exercises per student
- 40,433 theory pages online viewed
- average of 172 pages per student



Students still work outside contact hours, too



Students work during all days, but especially in the weekend



Course evaluation

- Subject not popular for all, but doable for all
- reduced postponement behavior (students work!)
- Fewer mistakes during laboratory work with mathematical calculations
  (think of diluting, pH calculation, etc.)
- Students have a need for or just like
  - explanations from teacher, tutors, and peers
  - worked-out examples, with details about steps
  - more contact time

Explanation of intermediate steps

Precalculus B: Calculating with letters: Fractions with letters

Splitting and writing with a common denominator (exercise id: 1135)

Write the fraction

$$\frac{p}{p-5}+\frac{1}{p+5}$$

with a common denominator, then perform the addition or subtraction, and finally expand all brackets (or the last two steps in reverse order).

$$\frac{p}{p-5}+\frac{1}{p+5}=\frac{p(p+5)}{(p-5)(p+5)}+\frac{p-5}{(p-5)(p+5)}$$

writing with a common denominator

$$=\frac{p^2+5p}{p^2-5^2}+\frac{p-5}{p^2-5^2}$$

expansion of brackets

$$=\frac{p^2+6p-5}{p^2-25}$$

addition and simplification

- Digital environments support learning

In the words of a student:

“Lastly I would like to note that I liked very much the manner of assessment and the feedback in the sample exercises. This way I could quickly brush up my knowledge and it was easier for me to explain things to fellow students.”

Hypothesis:

Good students and motivated students get most out of this approach;
Weak students need more help as they already have trouble with simple skills or copy/paste from worked-out examples to exercises without understanding

3. What about models & modelling?

What is present in the basic math course?

- Application of math ad methods in contexts:
  chemical calculations, bio-electricity, …
- Study of basic models that are frequently used
  exponential, exponentially restricted growth, logistic growth
  also in contexts
  pharmacokinetics, neural modeling
- Discussion about the quality of models:
  descriptive, predictive, explanatory
- Hardly simulations of models (done in other courses)
  but here in will use COACH for this purpose

Application of methods in contexts

- Linear functions
  - adult height prediction of females at menarche
  - 0-order reaction kinetics: $2\mathrm{N_2O} \xrightarrow{\mathrm{Au}} 2\mathrm{N_2} + \mathrm{O_2}$
  - Widmark model of alcohol clearance:

$$BAC(t) = BAC(0) - \beta \cdot t$$

Important to describe dependency of parameters on other quantities

$$BAC(t) = \frac{D}{r \cdot W} - \beta \cdot t$$

where *D* is the alcohol dosis, *W* is body weight, and *r* depends on gender.

- Powers
  - Allometry:

    primate brain weight *B* vs body weight *G*: $B = 0.11482G^{0.75}$

  - Solubility calculations: $CaF_2 \rightleftarrows Ca^{2+} + 2F^-$

$$K_s = [Ca^{2+}] \cdot [F^-]^2$$

Let *x* mol/L substance dissolve: $[Ca^{2+}] = x, [F^-] = 2x$

Thus:

$$K_s = x \cdot (2x)^2 = 4x^3$$

- Polynomials

$CaF_2 \rightleftarrows Ca^{2+} + 2F^-$ in presence of 1.6M KF

$$K_s = [Ca^{2+}] \cdot [F^-]^2$$

Let x mol/L substance dissolve: $[Ca^{2+}] = x, [F^-] = 2x + 1.6$

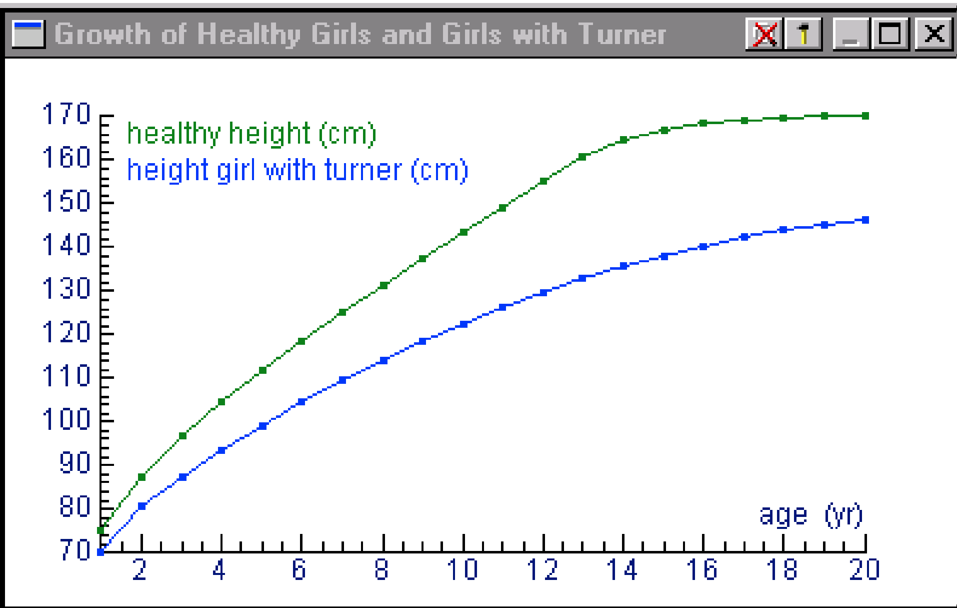
Thus:

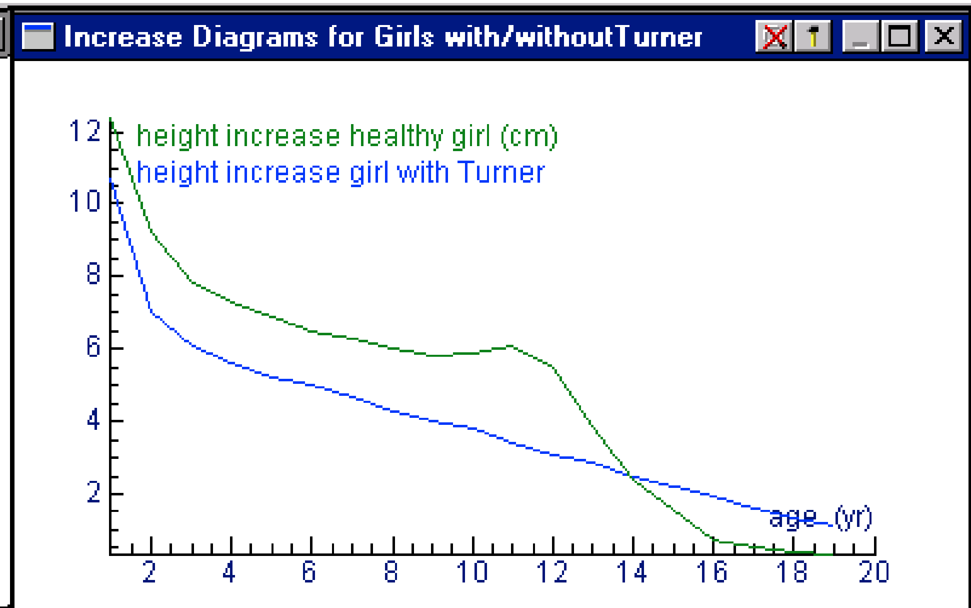
$$K_s = x \cdot (2x + 1.6)^2 \approx x \cdot 1.6^2$$

because x will be small

Symbolic approximation are important!

- Height growth of girls with Turner’s syndrome





- Exponential functions and logarithms
  - $pH = -\log_{10}([\mathrm{H_3O^+}])$

    primate brain weight *B* vs body weight *G*: $B = 0.11482G^{0.75}$

  - Acid-base calculations: $\mathrm{HAc} + \mathrm{H_2O} \rightleftarrows [\mathrm{H_3O^+}] + \mathrm{Ac^-}$

$$pK_z = -\log_{10}(K_z) = -\log_{10}\left(\frac{[\mathrm{H_3O^+}]\cdot[\mathrm{Ac^-}]}{[\mathrm{HAc}]}\right)$$

  - Nernst potential of ions on sides of cell membrane

$$E_{ion} = -\frac{RT}{zF}\cdot ln\left(\frac{C_i}{C_e}\right)$$

    where C_i and C_e are the ion concentrations

Study of frequently used models

- Exponential models
  - Theoretical topics
    - Mathematical formulas (doubling time, half-life)
    - Change of units for parameters (different time scales)
    - Determination of parameters from data
    - Introduction to ODE
  - Applications (+ graphical modelling of ODEs)
    - Unlimited growth of microorgansims (bacteria, algae, …)
    - Collapse of the head of a beer
    - Pharmacokinetics: clearance of a drug from body
    - Discharge of a capacitor

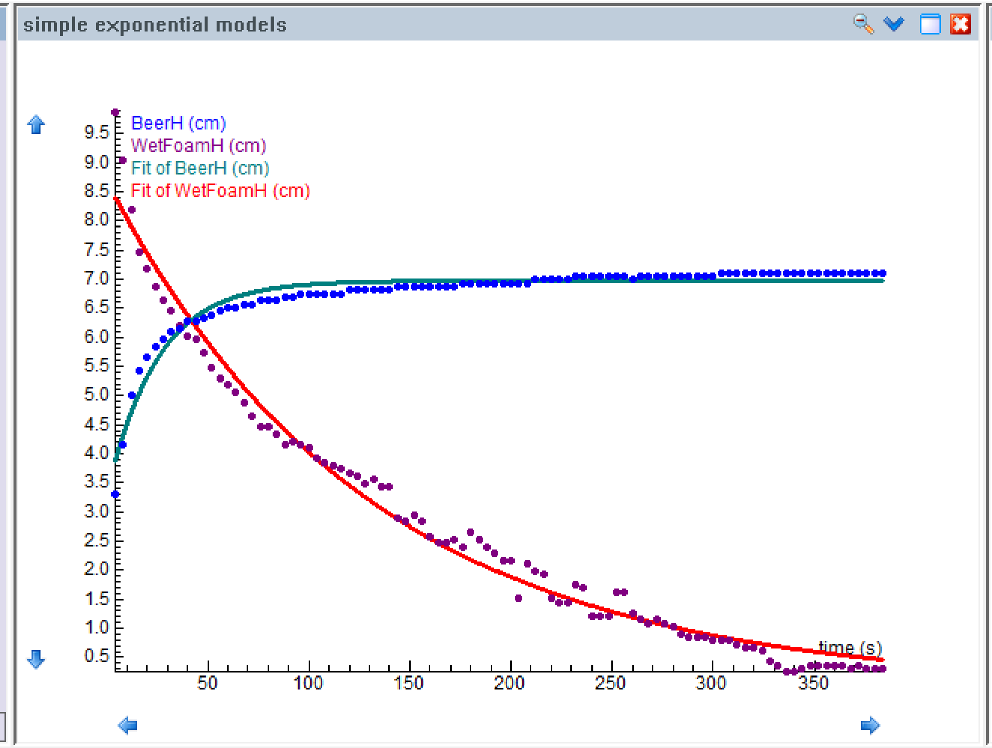
Collapse of the head of a beer:

Video analysis

Heck (2009). *Teaching Mathematics and its Applications, 28*(4), 164-179.

Video analysis as a tool to collect and analyse data:

[Change of the head of a beer](#) (low speed video)



Collapse of the head of a beer:

Various experimental models

Experimental modelling: **regression analysis** using

- exponential decay of foam height (WetFoamH)
- limited exponential growth of liquid height (BeerH)
- bi-exponential models of foam height and liquid height
- exponential decay of DryBeerH defined as

  DryFoamH = WetFoamH – (FinalBeerH - BeerH)

  in: Hackbarth, J. (2006). *Journal of the Institute of Brewing, 112*(1), 17-24

Next step: modelling based on systems of differential equations in a graphical system dynamics based approach

Collapse of the head of a beer :
Graphical models based on system dynamics

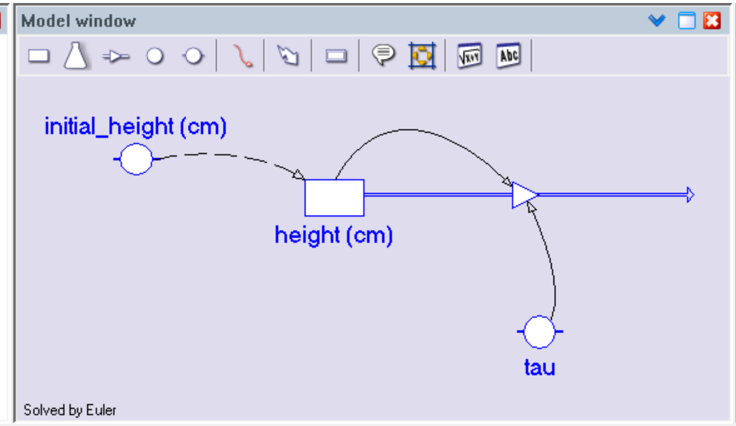
Graphical system dynamics based modelling of foam height

Model explanation

Exponential decay model for height h of beer froth:

$$h' = -h/\tau.$$

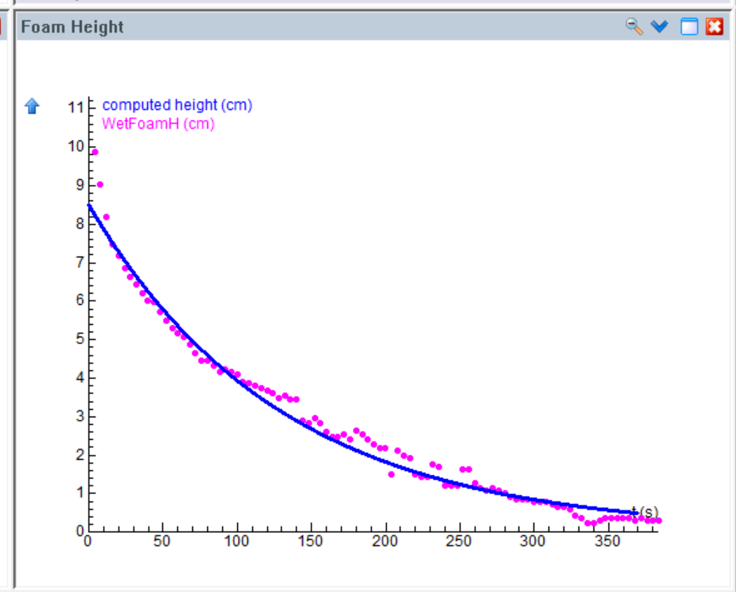
Exact solution: $h(t) = h_0 \cdot e^{-t/\tau}$



My Notes

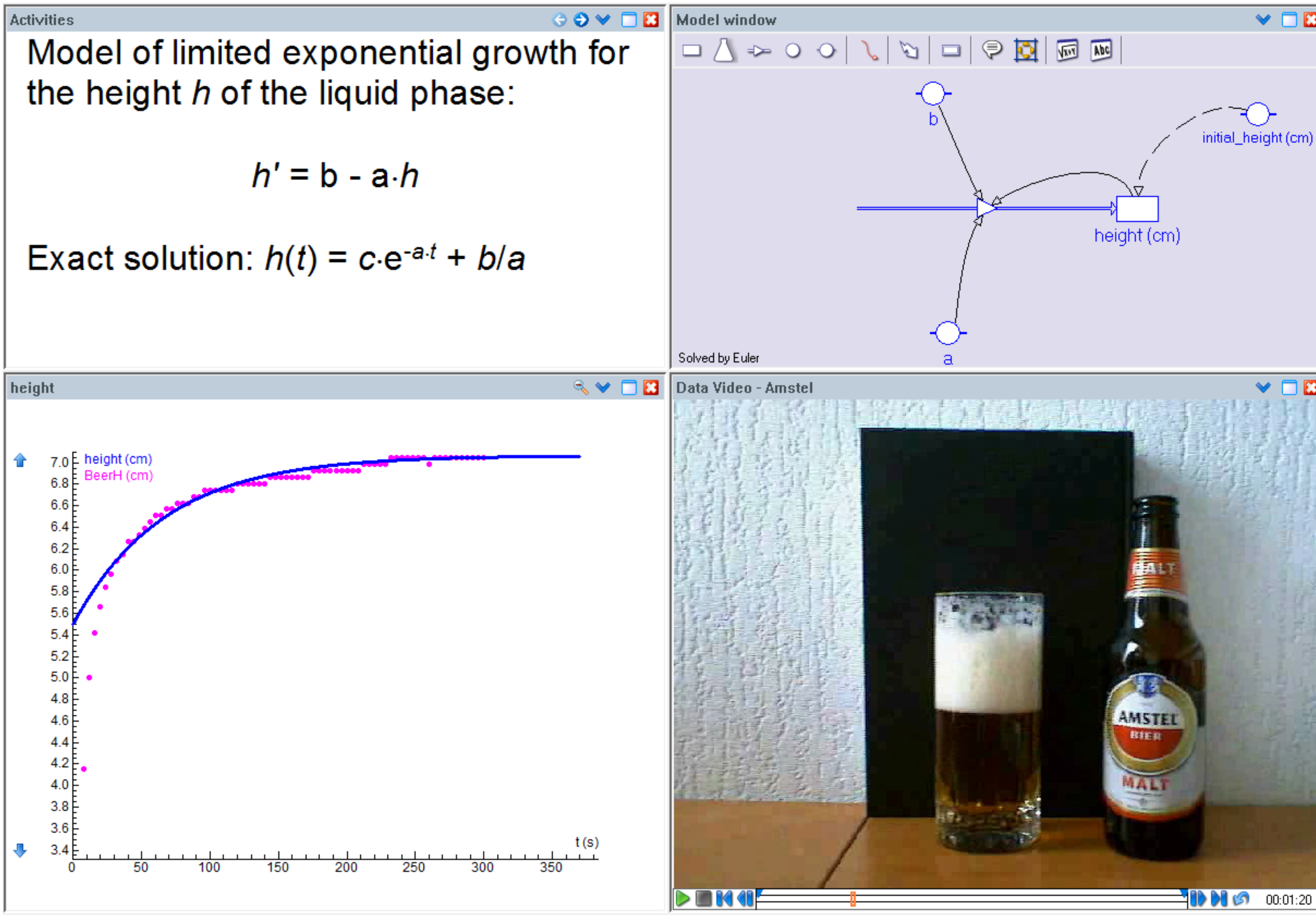
$\tau \approx 130$ sec

depending on
temperature of the beer,
temperature of the glass,
shape of the glass,
cleanness of the glass,
way of pourting beer in the glass,
composition of the glass...



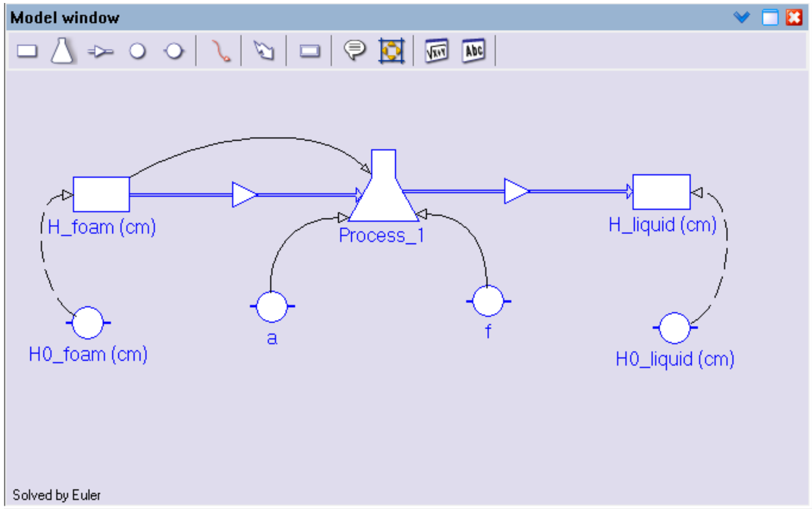
Collapse of the head of a beer:
Graphical models based on system dynamics

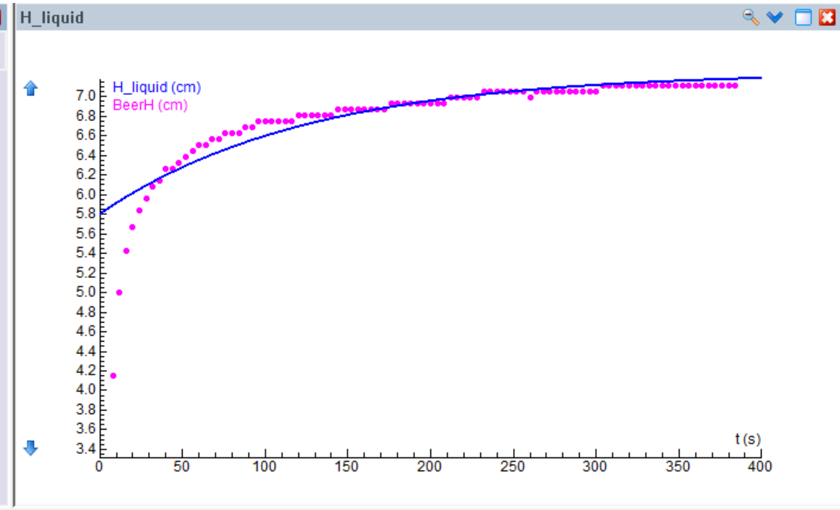
Graphical system dynamics based modelling of beer height



Collapse of the head of a beer:
Graphical models based on system dynamics

Mixed model



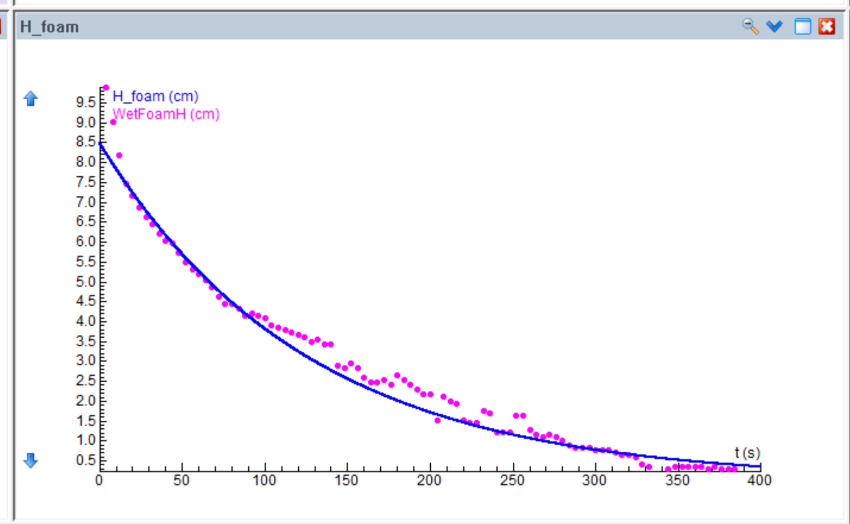


Model

System of differential equations for height of beer foam h_{foam} and liquid phase h_{liquid}:

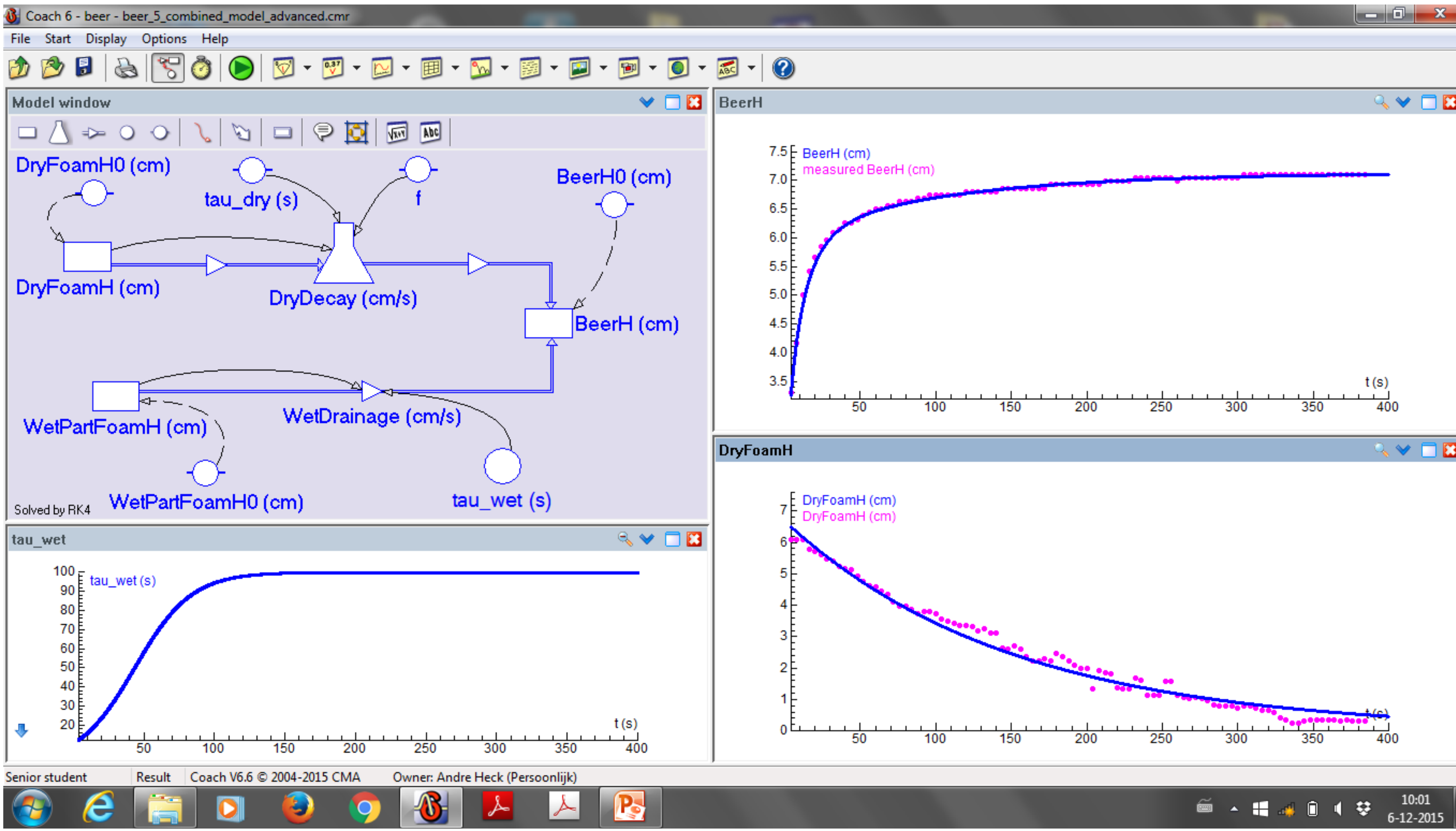
$$h'_{foam} = -\,a \cdot h_{foam}$$

$$h'_{liquid} = -\,f \cdot h'_{foam}$$



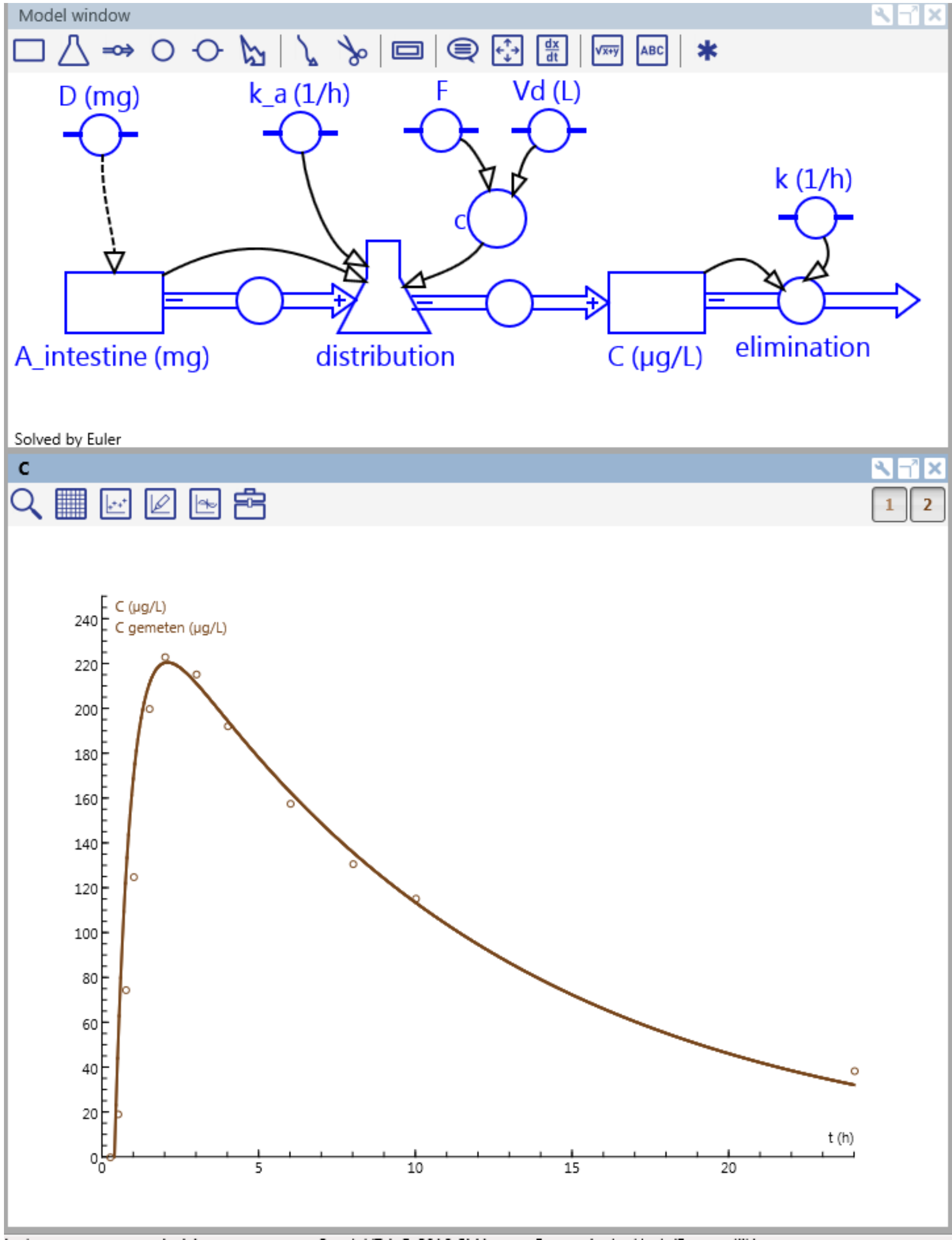
Collapse of the head of a beer: Advanced model of beer and foam height

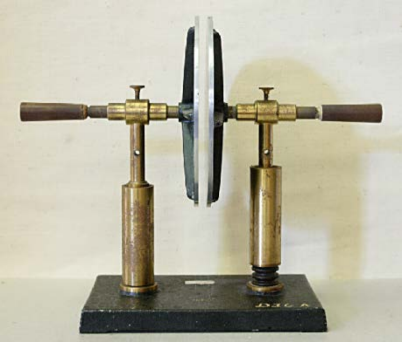
Advanced model



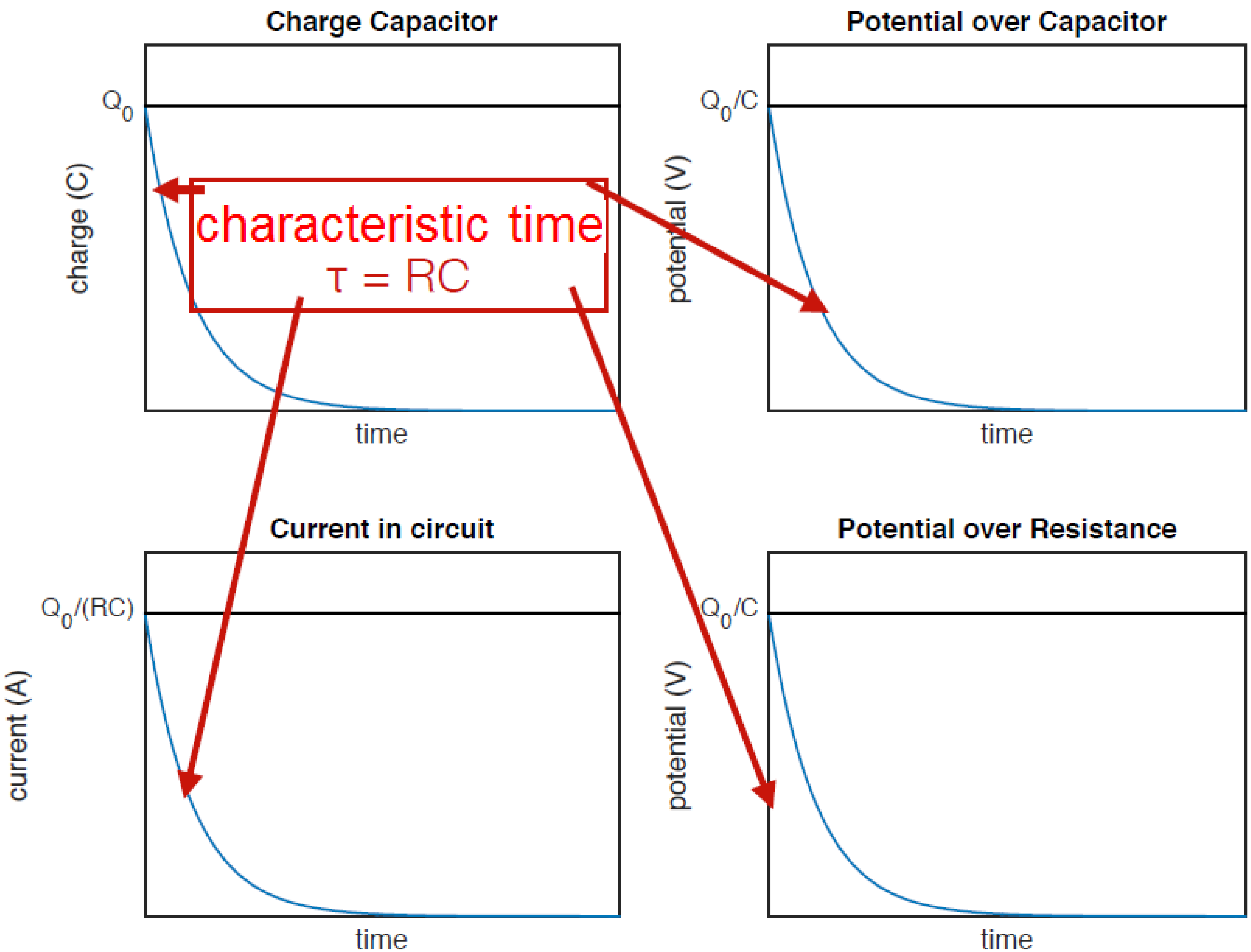
Intake and clearance of extasy

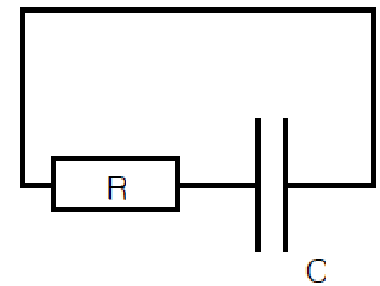
Bi-exponential model for
- oral drug intake
  (exponential decay from small intestine)
- clearance of drug from body system
  (exponential decay)





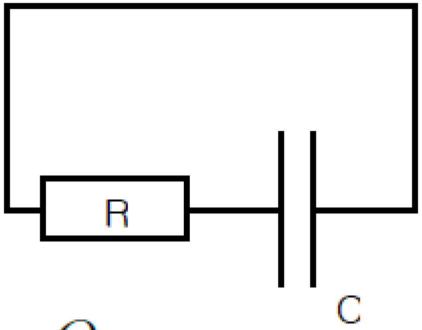
Discharge of a capacitor





$$C = \frac{Q}{V}$$

Mathematical model of discharge

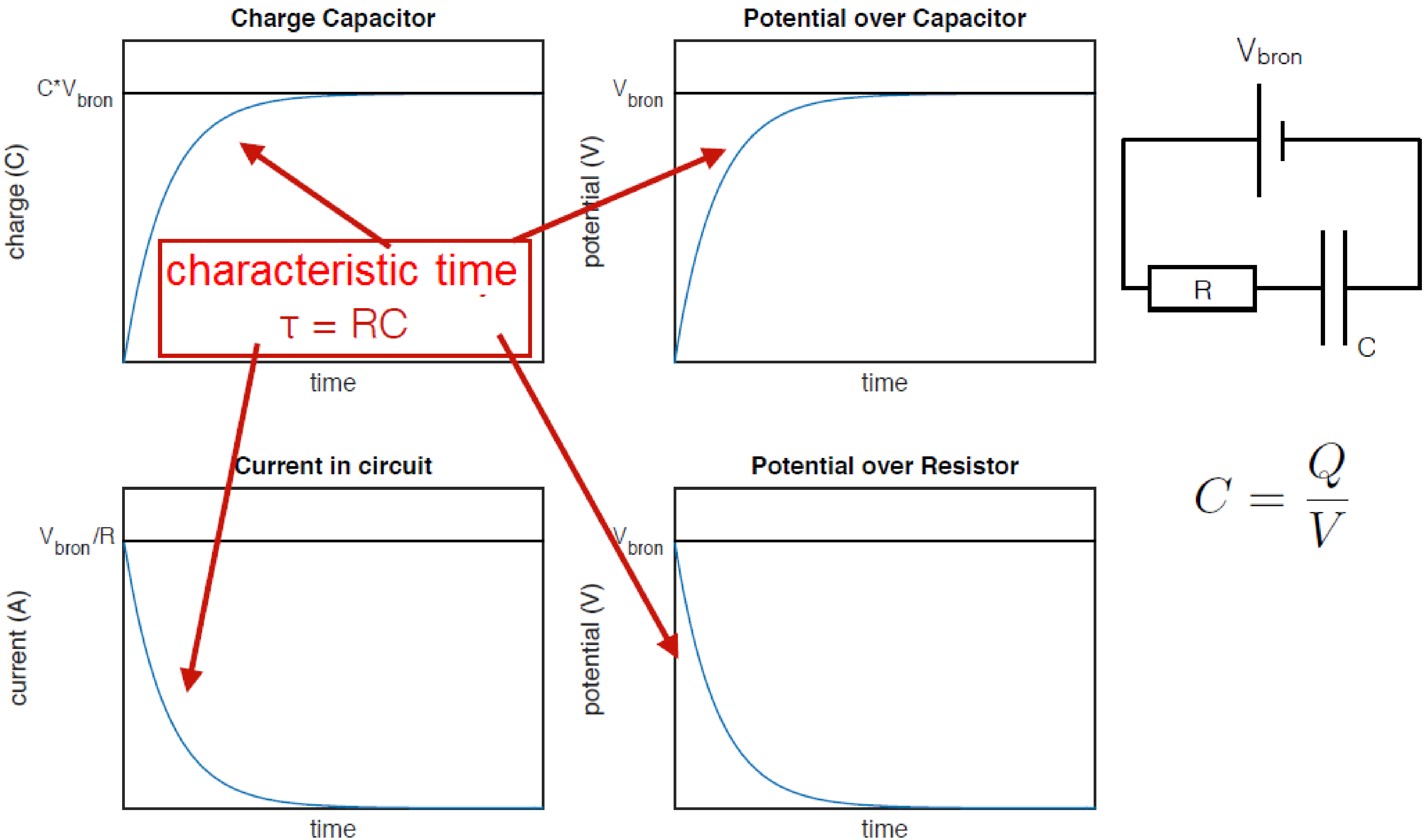


- Kirchhoff's law and Ohm's law: $V_R + V_C = IR + \frac{Q}{C} = 0$
- Substitution of $I(t) = Q'(t)$ gives: $R\frac{dQ}{dt} + \frac{Q}{C} = 0$
- So: $\frac{dQ}{dt} = -\frac{1}{RC}Q$
- Also: $\frac{dQ}{dt} = -\frac{Q}{\tau}$ with characteristic time $\tau = RC$
- Differential equation of exponential decay!
- Solution: $Q(t) = Q_0 e^{-\frac{t}{\tau}}$

Study of frequently used models

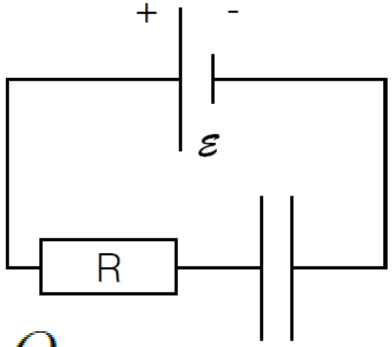
- Exponentially limited models
  - Theoretical topics
    - Mathematical formulas (time constant, equilibrium)
    - Determination of parameters from data
    - Introduction to ODE
  - Applications (+ graphical modelling of ODEs)
    - Model of liquid phase in collapse of beer head
    - Reaction kinetics for $A \rightleftarrows B$
    - Pharmacokinetics: repeated drug administration, infusion
    - Charging a capacitor
    - LIF neural model

Charging a capacitor



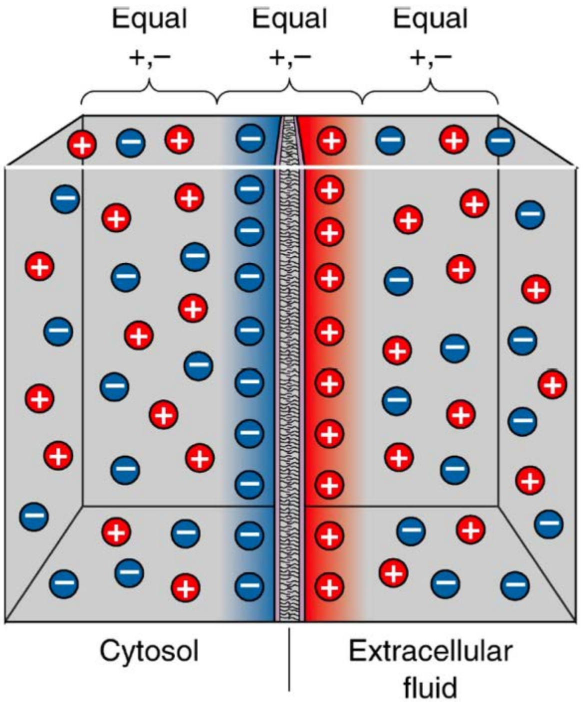
$$C = \frac{Q}{V}$$

Mathematical model of charging



- Kirchhoff's law and Ohm's law: $V_R + V_C = IR + \frac{Q}{C} = \mathcal{E}$
- Substitution of $I(t) = Q'(t)$ gives: :$R\frac{dQ}{dt} + \frac{Q}{C} = \mathcal{E}$
- So: $\frac{dQ}{dt} + \frac{Q}{RC} = \frac{\mathcal{E}}{R}$
- Also: $\frac{dQ}{dt} = -\frac{Q}{\tau} + \frac{\mathcal{E}}{R}$ with characteristic time $\tau = RC$
- Differential equation of exponentially limited growth!
- Initial value: $Q(0) = 0$ Solution: $Q(t) = \mathcal{E}C\left(1 - e^{-\frac{t}{\tau}}\right)$
- Current: $I(t) = \frac{dQ}{dt} = \frac{\mathcal{E}C\left(1 - e^{-\frac{t}{RC}}\right)}{dt} = \frac{\mathcal{E}}{R}e^{-\frac{t}{RC}}$

Electric model of cell membrane

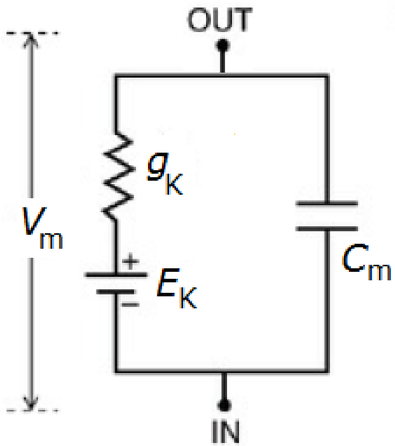


- Membrane is a capacitor because semipermeability of ion channel gives a charge division on both sides of the membrane.

- $C_m \approx 1 \mu F/cm^2$

- Ion channel 'operates' as a battery with a resistor in series.

  Electric analogue:
  parallel ion channel and capacitor



Membrane potential for two ion channels: K^+, Na^+

- Ohm's law:
$$\begin{aligned} I_{\mathrm{K}} &= g_{\mathrm{K}}(V_m - E_{\mathrm{K}}) \\ I_{\mathrm{Na}} &= g_{\mathrm{Na}}(V_m - E_{\mathrm{Na}}) \end{aligned}$$

- In rest: $I_{\mathrm{K}} + I_{\mathrm{Na}} = 0$

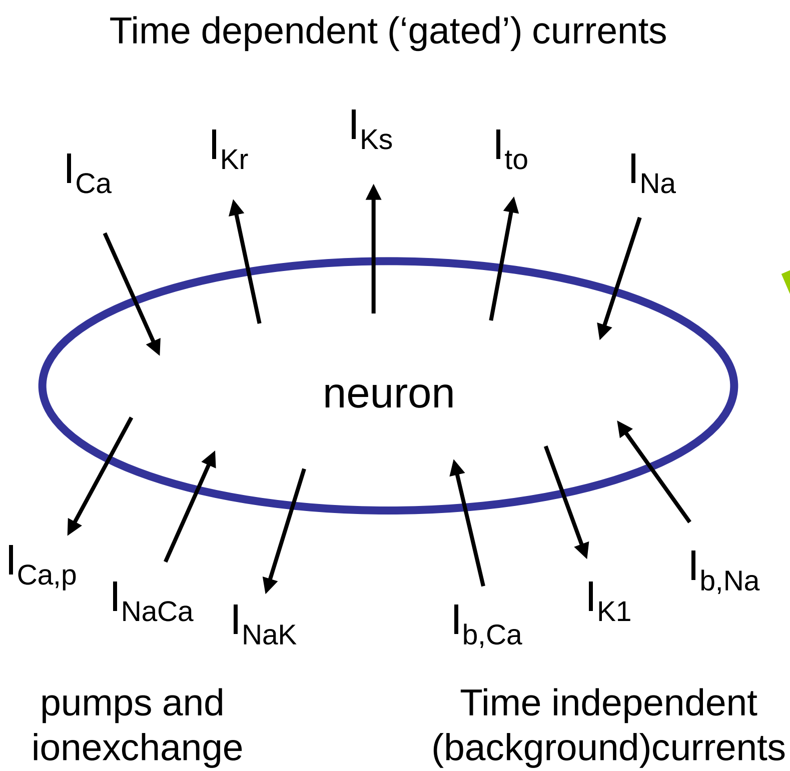
- Isolation of V_m:
$$V_m = \frac{g_{\mathrm{K}} E_{\mathrm{K}} + g_{\mathrm{Na}} E_{\mathrm{Na}}}{g_{\mathrm{K}} + g_{\mathrm{Na}}}$$

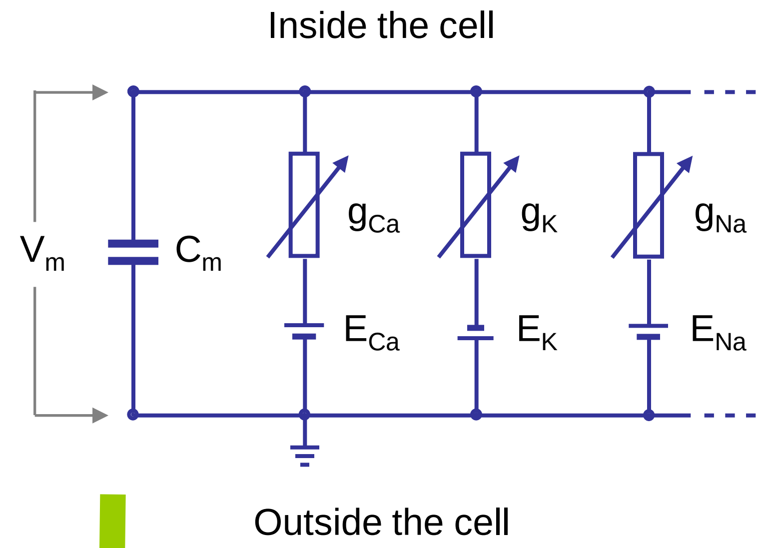
$$= \frac{g_{\mathrm{K}}}{g_{\mathrm{K}} + g_{\mathrm{Na}}} \cdot E_{\mathrm{K}} + \frac{g_{\mathrm{Na}}}{g_{\mathrm{K}} + g_{\mathrm{Na}}} \cdot E_{\mathrm{Na}}$$

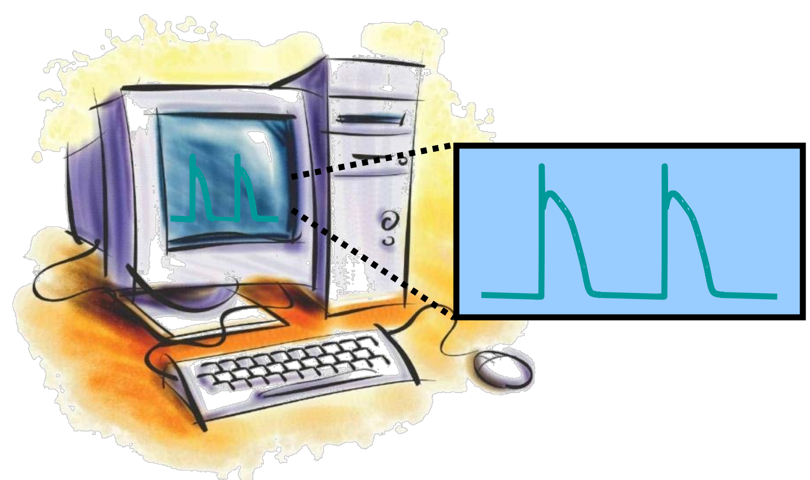
- Equation with stimulus I_{stim}

$$I_{\mathrm{stim}} = C_m \cdot \frac{dV_m}{dt} + g_K(V - E_K) + g_{Na}(V - E_{Na})$$

Equivalent electric model for excitable cell

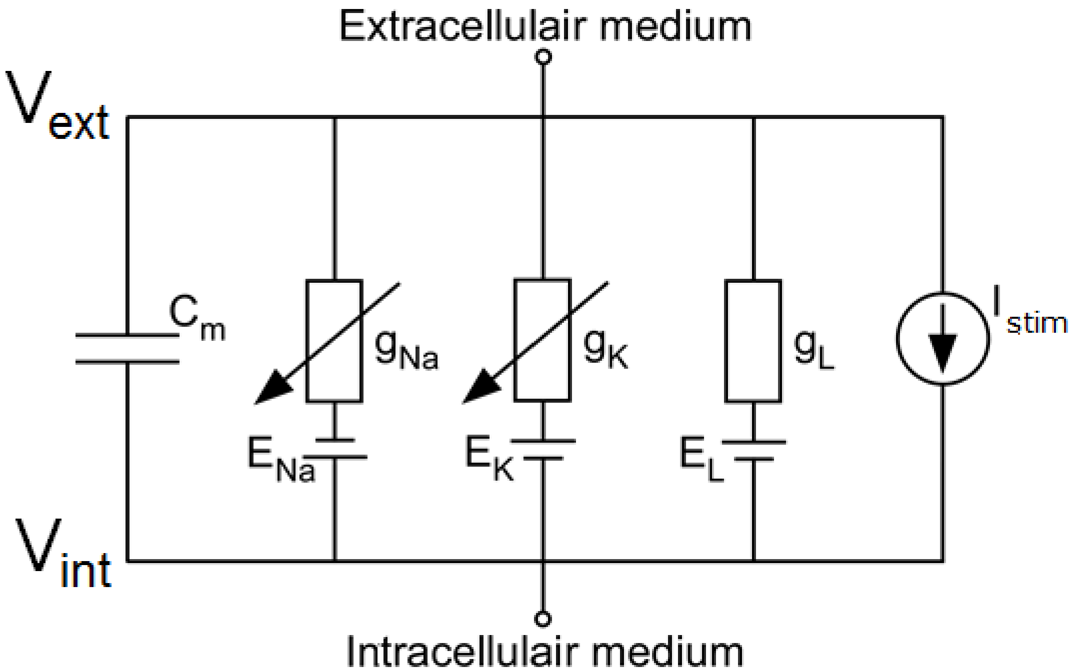






Conductivity of relevant ions is voltage- and time-dependent and leads to an actiopotential

Model van Hodgkin en Huxley



$$V_m = V_{int} - V_{ext}$$

$$C_m \frac{dV_m}{dt} + I_{Na} + I_K + I_L = I_{stim}$$

$$I_{\text{ion}} = g_{\text{ion}} \cdot (V_m - E_{\text{ion}})$$

Conductivity of Kalium

- Kalium current: $I_K = g_K(V - E_{\mathrm{K}})$

- Idea of Hodgkin and Huxley:

  $g_{\mathrm{K}} = \overline{g_{\mathrm{K}}} \cdot n^4$ where *n*(*t*) is the fraction open K+ channels

- *n*(*t*) satisfies the following ODE:

  $$\frac{dn}{dt} = \alpha_n \cdot (1-n) - \beta_n \cdot n$$

- This is ODE of anexponentially limited model with solution:

  $n(t) = n_\infty \cdot \left(1 - \exp(-\frac{t}{\tau_n})\right)$ with voltage-dependent params.

  $$n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n} \quad \text{en} \quad \tau_n = \frac{1}{\alpha_n + \beta_n}$$

Conductivity of sodium

- Natrium current: $I_{\mathrm{Na}} = g_{\mathrm{Na}}(V - E_{\mathrm{Na}})$

- Idea of Hodgkin and Huxley:
  three channel states: open, inactive, closed
  via two gating mechanisms

  $$g_{\mathrm{Na}} = \overline{g_{\mathrm{Na}}} \cdot m^3 h$$

- *m*(*t*) and *h*(*t*) satisfy:

  $$\frac{dm}{dt} = \alpha_m(1-m) - \ \beta_m m \qquad \text{en} \qquad \frac{dh}{dt} = \alpha_h(1-h) - \ \beta_h h$$

- Again ODEs of exponentially limited model

- Parameters depend on membrane potential

- Simulation in Coach

Simplified models

- Wilson model: $h = 1 - n$, $m(t) = m_{\infty}(V)$, natrium and leakage channel combined into a new single natrium channel.
  This leads to system of ODES in two variables
  Therefore phane plane analysis can be done

- FitzHugh-Nagumo model:
  two variable system with (fast) voltage variable *v* and (slow) recovery variable *w*:

$$\frac{dv}{dt} = f(v) - w + I_{\mathrm{stim}}$$

$$\frac{dw}{dt} = \varepsilon \cdot \left(v + \beta - \gamma \cdot w\right)$$

$$f(v) = v - \frac{1}{3}v^3$$

- LIF model: leaky integrate-and-fire model (ignore peaks)

$\tau \cdot \frac{dV}{dt} = V - \frac{I_{stim}}{g}$, when V reaches V_{th}, a reset of V to V_{rest}

Simplified models

- Izhekevich model: $$\frac{dV}{dt} = 0.04V^2 + 5V + 140 - U + I_{\text{stim}}$$
$$\frac{dU}{dt} = a \cdot \left(b \cdot V - U \right)$$

  when V reaches threshold V_{th}, then V reset to c and U reset to d

- Reduces models are used in simulations of neural networks

4.Conclusion

Models are used in many contexts

- for detailed replicates of a system to simulate dynamics
  - but a model is always an abstraction rather than a mirror of reality
  - nature is more complex than models pretend
- as method for research
  - tests of ideas or hypotheses (plausability/consequences)
  - analysis of data
  - Study of dynamic processes:
    stable/instable equilibria, feedback, hysteresis, tipping points

- Mathematical equations "say" more than surrounding text and provide template models

Compare the following discrete population model

$$N(t+1) = (1+b)\cdot\left((1-d)\cdot N(t)+m\right)$$

where

d: fraction of individuals dying per day

m: number of immigrants per day

b: number of offspring produced by day

with

each day a fraction d of all individuals die, while a fixed number of individuals m invade; subsequently all individuals produce b offspring before the population census on the next day

- Graphical models may be used by students for simulations, but at some moment they need to learn to program the
- Students must master mathematics skills needed for studying dynamic systems:
  - Algebraic skills
    - isolation of variables,
    - working with parameters,
    - solving equations
  - Mathematical reasoning skills (e.g. in phase plane analysis)
  - and more
- Modelling implies effort, use, and hopefully fun