Calculus for the Life Sciences I

Lecture Notes – The Derivative of e^x and $\ln(x)$

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Outline

Introduction

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- Special functions often arise in biological problems

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    - Biochemical Kinetics

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  - Population dynamics

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  - Population dynamics
- Need the derivatives for e^x and $\ln(x)$
- Find maxima, minima, and points of inflection

Fluoxetine (Prozac) 1

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- This drug is used to treat depression, obsessive compulsive disorder, and a number of other neurological disorders
- It works by preventing serotonin from being reabsorbed too rapidly from the synapses between nerve cells, prolonging its availablity, which improves the patient's mood

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- Fluoxetine and norfluoxetine are eliminated from the brain with characteristic **half-lives** of 1-4 days and 7-15 days, respectively

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- Drugs metabolized into another active form make modeling more complex
- Models below examine first order kinetic models for the concentrations of fluoxetine $(F(t))$ and norfluoxetine $(N(t))$ in the blood

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- The drug decays exponentially with a characteristic half-life

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- Solving this equation for k,

$$e^{1.5k} = 2 \quad \text{or} \quad k = \ln(2)/1.5 = 0.462$$

Fluoxetine (Prozac)

Model for Fluoxetine

A good model for blood plasma concentration of fluoxetine is

$$F(t) = 21\, e^{-0.462t}$$

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- Pharmokinetic models often are composed of the difference of two decaying exponentials

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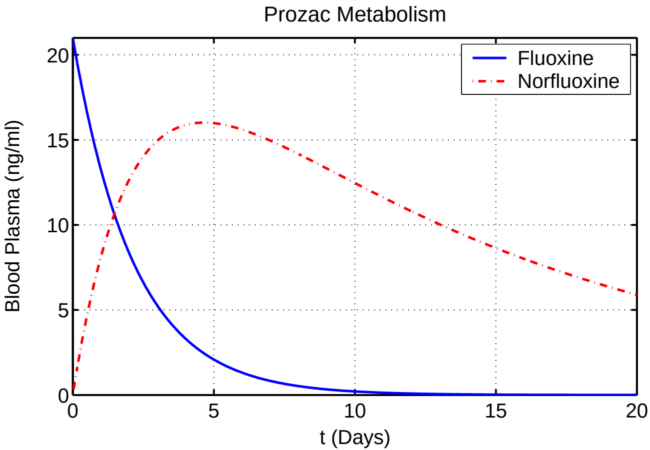
Graph of Fluoxetine and Norfluoxetine



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- To solve these problems, we need to learn the formula for the derivative of the exponential function

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From the definition of the derivative and using the properties of exponentials

$$\frac{d}{dx}(e^x) = \lim_{h\to 0} \frac{e^{x+h} - e^x}{h} = e^x \lim_{h\to 0} \frac{e^h - 1}{h} = e^x$$

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General rule for the derivative of e^{kx}

The derivative of e^{kx} is

$$\frac{d}{dx}(e^{kx}) = k\,e^{kx}$$

Example – Exponential Function

Example: Find the derivative of

$$f(x) = 5\,e^{-3x}$$

Solution: From our rule of differentiation and the formula above

$$f'(x) = -15\,e^{-3x}$$

Application of the Derivative to Prozac Model

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$$F'(t) = (-0.462)21\,e^{-0.462t} = -9.702\,e^{-0.426t}$$

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The rate of change of blood plasma concentration of fluoxetine at times $t = 2$ and 10 is

$$\begin{aligned} F'(2) &= -9.702\,e^{-0.462(2)} = -3.85 \text{ ng/ml/day} \\ F'(10) &= -9.702\,e^{-0.462(10)} = -0.0956 \text{ ng/ml/day} \end{aligned}$$

Application of the Derivative to Norfluoxetine Model

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Solution: The derivative is

$$\begin{aligned} N'(t) &= 27.5(-0.077\,e^{-0.077t} + 0.462\,e^{-0.426t}) \\ &= 12.705\,e^{-0.462t} - 2.1175\,e^{-0.077t} \end{aligned}$$

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The rate of change of blood plasma concentration of norfluoxetine at times $t = 2$ and 10 is

$$\begin{aligned} N'(2) &= 12.705\, e^{-0.462(2)} - 2.1175\, e^{-0.077(2)} = 3.23 \text{ ng/ml/day} \\ N'(10) &= 12.705\, e^{-0.462(10)} - 2.1175\, e^{-0.077(10)} = -0.855 \text{ ng/ml/day} \end{aligned}$$

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The maximum blood plasma concentration of norfluoxetine is

$$N(t_{max}) = 16.01 \text{ ng/ml}$$

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$$0.385\, t = \ln(36) = 2\,\ln(6) \quad \text{and} \quad t_{poi} = 9.308 \text{ days}$$

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$$0.385\, t = \ln(36) = 2\,\ln(6) \quad \text{and} \quad t_{poi} = 9.308 \text{ days}$$

with blood plasma concentration of norfluoxetine at

$$N(t_{poi}) = 12.91 \text{ ng/ml} \quad \text{and} \quad N'(t_{poi}) = -0.862 \text{ ng/ml/day}$$

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Graphing an Exponential: Consider

$$y(x) = 2\,e^{-0.2x} - 1$$

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- Find its derivative

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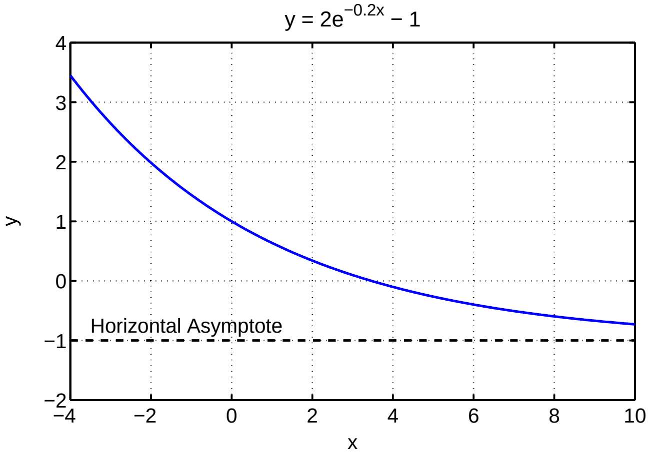
For large values of x, the exponential function decays to zero

Thus, there is a horizontal asymptote to the right with

$$y = -1$$

Example – Graphing an Exponential

Graph: $y(x) = 2\,e^{-0.2x} - 1$



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- This function is always decreasing

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- **Model for Injection of a Drug**

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  - Concentration of the drug, $k(t)$
  - Total dose, A_0
  - Rate of clearance, q

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- New drug delivery devices

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- Several long term birth control devices
  - Devices deliver the hormones estrogen and progesterone
  - Delivery gives a more uniform level of the hormones over extended periods of time to prevent pregnancy
- New drug delivery devices
  - Diabetes sufferers could receive a more uniform level of insulin

Example – Polymer Drug Delivery System 2

Polymer Drug Delivery System:

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- New drug delivery devices
  - Diabetes sufferers could receive a more uniform level of insulin
  - Chemotherapeutic drugs to cancer patients could extend over a much longer period of time at lower doses to maximize their efficacy

Example – Polymer Drug Delivery System 3

Model for a Polymer Drug Delivery Device:
Mathematically, this is described by two decaying exponentials

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- The amounts of drug are the same when

$$A_0 = \frac{C_0}{r}$$

Example – Polymer Drug Delivery System 4

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Example – Polymer Drug Delivery System 4

Drug Delivery: This example examines the same amount of drug delivered by injection and a polymer delivery device

- Suppose the drug is injected

$$k(t) = 1000\, e^{-0.2t}$$

- $k(t)$ is a concentration in mg/dl and the time t is in days
- The same amount of drug is delivered by a polymer drug delivery device satisfies

$$c(t) = 10(e^{-0.01t} - e^{-0.2t})$$

- $c(t)$ is a concentration in mg/dl

Example – Polymer Drug Delivery System

Drug Delivery: Comparing the injected and polymer delivered drug systems

Example – Polymer Drug Delivery System 5

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Example – Polymer Drug Delivery System 5

Drug Delivery: Comparing the injected and polymer delivered drug systems

- Find the rate of change in concentration for both $k(t)$ and $c(t)$ at $t = 5$ and 20
- Determine the maximum concentration of $c(t)$ and when it occurs
- Graph each of these functions

Example – Polymer Drug Delivery System 6

Solution: Since $k(t) = 1000\,e^{-0.2t}$, the derivative is

$$k'(t) = (-0.2)1000\,e^{-0.2t} = -200\,e^{-0.2t}$$

Example – Polymer Drug Delivery System 6

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- $$k'(5) = -200\,e^{-0.2(5)} = -73.58 \text{ mg/dl/day}$$

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Example – Polymer Drug Delivery System

Solution (cont): Since $c(t) = 10(e^{-0.01t} - e^{-0.2t})$, the derivative is

$$c'(t) = 10(-0.01\, e^{-0.01t} - (-0.2)e^{-0.2t}) = 2\, e^{-0.2t} - 0.1\, e^{-0.01t}$$

Example – Polymer Drug Delivery System

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- The rate of change of the drug concentrations at times $t = 5$ and 20 for the injected drug is
- $$c'(5) = 2\,e^{-0.2(5)} - 0.1\,e^{-0.01(5)} = 0.64 \text{ mg/dl/day}$$

Example – Polymer Drug Delivery System 7

Solution (cont): Since $c(t) = 10(e^{-0.01t} - e^{-0.2t})$, the derivative is

$$c'(t) = 10(-0.01\,e^{-0.01t} - (-0.2)e^{-0.2t}) = 2\,e^{-0.2t} - 0.1\,e^{-0.01t}$$

- The rate of change of the drug concentrations at times $t = 5$ and 20 for the injected drug is
- $$c'(5) = 2\,e^{-0.2(5)} - 0.1\,e^{-0.01(5)} = 0.64 \text{ mg/dl/day}$$
- $$c'(20) = 2\,e^{-0.2(20)} - 0.1\,e^{-0.01(20)} = -0.045 \text{ mg/dl/day}$$

Example – Polymer Drug Delivery System 8

Solution for Maximum for $c(t)$: Since the derivative is

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Thus,

$$e^{-0.01t+0.2t} = e^{0.19t} = 20$$

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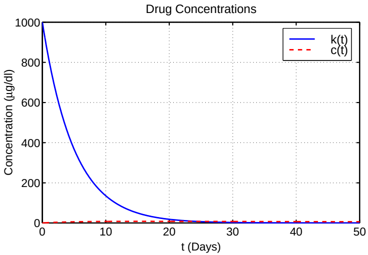
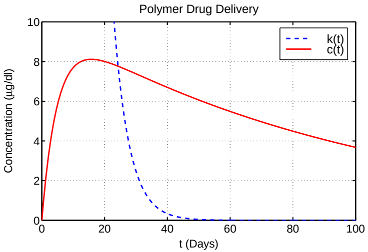
The maximum occurs at $c(15.767) = 8.11\ \mu\text{g/dl}$

Example – Polymer Drug Delivery System

Graph: Drug Delivery





Example – Polymer Drug Delivery System

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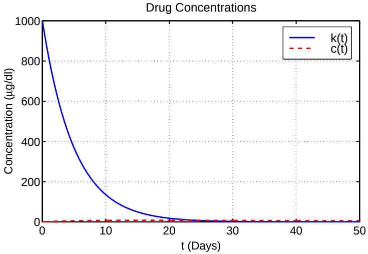
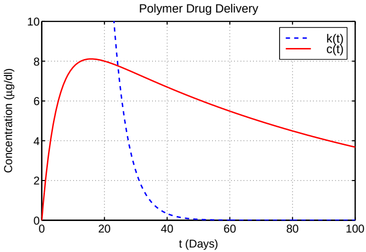
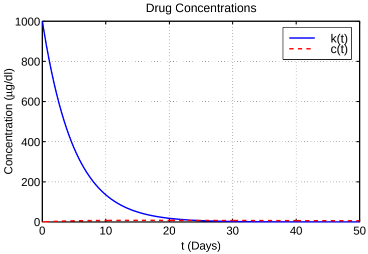


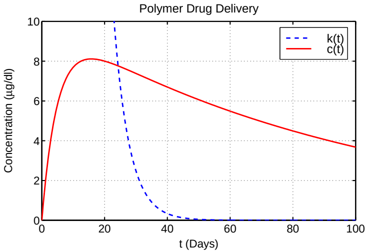


The polymer delivered drug over a longer period of time

Example – Polymer Drug Delivery System

Graph: Drug Delivery





The polymer delivered drug over a longer period of time

These graphs show the obvious advantages of the time released drug if it has serious side effects or toxicity

Height and Weight Relationship for Children 1

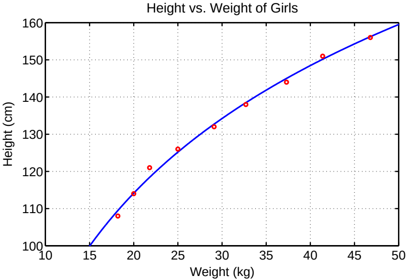
Height and Weight Relationship for Children:

age(years)	height(cm)	weight(kg)
5	108	18.2
6	114	20.0
7	121	21.8
8	126	25.0
9	132	29.1
10	138	32.7
11	144	37.3
12	151	41.4
13	156	46.8

Height and Weight Relationship for Children 2

Ehrenberg Model: Logarithmic relationship

$$H(w) = 49.5\ \ln(w) - 34.14$$



Want to find the find the **rate of change of height with respect to weight** for the average girl

Derivative of $\ln(x)$

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The derivative of the natural logarithm, $\ln(x)$, is given by the formula

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This relationship is most easily demonstrated after learning the Fundamental Theorem of Calculus in Math 122, which centers about the integral

Derivative of Ehrenberg Model

Derivative of Ehrenberg Model: The Ehrenberg model for the previous data

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- At $w = 20$ kg

$$H'(20) = \frac{49.5}{20} = 2.475 \text{ cm/kg}$$

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- At $w = 49.5$ kg

$$H'(49.5) = \frac{49.5}{49.5} = 1 \text{ cm/kg}$$

Example – Derivative of Logarithm

Example: Find the derivative of

$$f(x) = \ln(x^2)$$

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Example – Logarithm Function 1

Example: Consider the following function

$$y = x - \ln(x)$$

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- Find the first and second derivatives of this function

Example – Logarithm Function 1

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Example – Logarithm Function 1

Example: Consider the following function

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- Find the first and second derivatives of this function
- Find any local extrema
- Graph the function

Example – Logarithm Function 2

Solution: The function $y = x - \ln(x)$ has the derivative

$$\frac{dy}{dx} = 1 - \frac{1}{x} = \frac{x-1}{x}$$

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Note that since $y''(x) > 0$, this function is concave upward

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Solution (cont): Graphing the Function

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There is an **extremum** at **(1,1)**

Example – Logarithm Function 4

Solution (cont): Graphing the Function

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Solution (cont): Graphing the Function

- Since the second derivative is always positive

Example – Logarithm Function 4

Solution (cont): Graphing the Function

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Example – Logarithm Function

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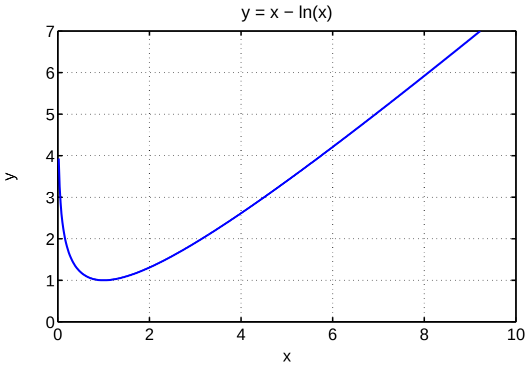

Example – von Bertalanffy Model 1

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Problem 1: The von Bertalanffy equation is

$$W(a) = 20.2(1 - e^{-0.019a})$$

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- Find the rate of change of weight, W, with respect to the age, a
- Graph the solution of the von Bertalanffy equation

Example – von Bertalanffy Model 2

Solution 1: **von Bertalanffy Model** is written

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Differentiating the model with respect to age, a, gives

$$\frac{dW}{da} = -20.2(-0.019)e^{-0.019a} = 0.3838\,e^{-0.019a} \text{ kg/yr}$$

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Differentiating the model with respect to age, a, gives

$$\frac{dW}{da} = -20.2(-0.019)e^{-0.019a} = 0.3838\, e^{-0.019a} \text{ kg/yr}$$

This function is monotonically increasing (as we would expect for growth of a fish)

Example – von Bertalanffy Model 3

Solution 1 (cont): Graph of **von Bertalanffy Model**

$$W(a) = 20.2 - 20.2\, e^{-0.019a}$$

Example – von Bertalanffy Model 3

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- This equation goes through the origin

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Example – von Bertalanffy Model 3

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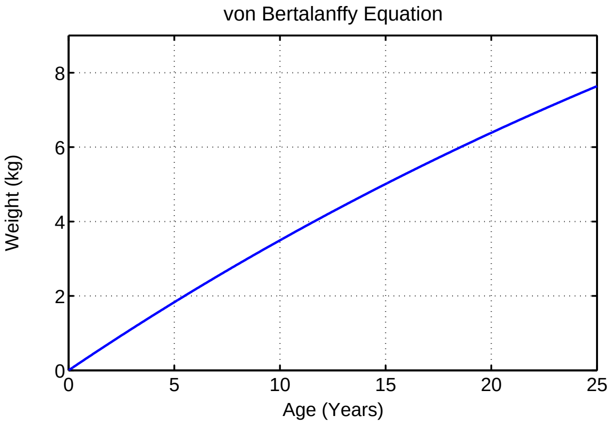
- This equation goes through the origin
- For large values of a, the exponential decays to zero
- Thus, there is a horizontal asymptote of $W = 20.2$
- Asymptotically the fish grows to a weight of **20.2 kg**

Example – von Bertalanffy Model

Solution 1 (cont): Graphing the von Bertalanffy Model



Example – Inverse von Bertalanffy Model 1

Problem 2: Inverse of **von Bertalanffy Model**

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- Solve the above equation for age, a, as a function of the weight, W
- Differentiate this function, finding the rate of change of age with respect to weight

Example – Inverse von Bertalanffy Model 1

Problem 2: Inverse of **von Bertalanffy Model**

$$W(a) = 20.2 - 20.2\,e^{-0.019a}$$

- Solve the above equation for age, a, as a function of the weight, W
- Differentiate this function, finding the rate of change of age with respect to weight
- Graph this function showing any intercepts and asymptotes

Example – Inverse von Bertalanffy Model 2

Solution 2: The **von Bertalanffy Model**

$$W(a) = 20.2 - 20.2\, e^{-0.019a}$$

$$20.2\, e^{-0.019a} = 20.2 - W$$

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$$W(a) = 20.2 - 20.2\,e^{-0.019a}$$

$$\begin{aligned} 20.2\,e^{-0.019a} &= 20.2 - W \\ e^{0.019a} &= \frac{20.2}{20.2 - W} \end{aligned}$$

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$$\begin{aligned} 20.2\, e^{-0.019a} &= 20.2 - W \\ e^{0.019a} &= \frac{20.2}{20.2 - W} \\ a &= \frac{1}{0.019} \ln\left(\frac{20.2}{20.2 - W}\right) \end{aligned}$$

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e^{0.019a} &= \frac{20.2}{20.2 - W} \\
a &= \frac{1}{0.019}\ln\left(\frac{20.2}{20.2 - W}\right) \\
a(W) &= \frac{1}{0.019}\left(\ln(20.2) - \ln(20.2 - W)\right)
\end{aligned}$$

Example – Inverse von Bertalanffy Model 2

Solution 2: The **von Bertalanffy Model**

$$W(a) = 20.2 - 20.2\, e^{-0.019a}$$

$$\begin{aligned}
20.2\, e^{-0.019a} &= 20.2 - W \\
e^{0.019a} &= \frac{20.2}{20.2 - W} \\
a &= \frac{1}{0.019} \ln\left(\frac{20.2}{20.2 - W}\right) \\
a(W) &= \frac{1}{0.019} \left(\ln(20.2) - \ln(20.2 - W)\right)
\end{aligned}$$

The age, a, as a function of the weight, W, is

$$a(W) = 158.2 - 52.63 \ln(20.2 - W)$$

Example – Inverse von Bertalanffy Model 3

Solution 2 (cont): The **Inverse von Bertalanffy Model**

$$a(W) = 158.2 - 52.63 \ln(20.2 - W)$$

cannot be directly differentiated without the **chain rule**

Example – Inverse von Bertalanffy Model 3

Solution 2 (cont): The **Inverse von Bertalanffy Model**

$$a(W) = 158.2 - 52.63\ \ln(20.2 - W)$$

cannot be directly differentiated without the **chain rule**

Consider the substitution, $Z = 20.2 - W$

Example – Inverse von Bertalanffy Model 3

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$$a(W) = 158.2 - 52.63\ \ln(20.2 - W)$$

cannot be directly differentiated without the **chain rule**

Consider the substitution, $Z = 20.2 - W$
(Note that $\frac{dZ}{dW} = -1$)

Example – Inverse von Bertalanffy Model 3

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Consider the substitution, $Z = 20.2 - W$
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$$a(Z) = 158.2 - 52.63\ \ln(Z)$$

Example – Inverse von Bertalanffy Model 3

Solution 2 (cont): The **Inverse von Bertalanffy Model**

$$a(W) = 158.2 - 52.63\,\ln(20.2 - W)$$

cannot be directly differentiated without the **chain rule**

Consider the substitution, $Z = 20.2 - W$
(Note that $\frac{dZ}{dW} = -1$)

$$a(Z) = 158.2 - 52.63\,\ln(Z)$$

Differentiating

$$\frac{da}{dZ} = -52.63\frac{1}{Z}$$

Example – Inverse von Bertalanffy Model 4

Solution 2 (cont): The derivative of the **Inverse von Bertalanffy Model** is

$$\frac{da}{dZ} = -52.63\frac{1}{Z}$$

Example – Inverse von Bertalanffy Model 4

Solution 2 (cont): The derivative of the **Inverse von Bertalanffy Model** is

$$\frac{da}{dZ} = -52.63\frac{1}{Z}$$

We will show

$$\frac{da}{dW} = \frac{da}{dZ} \times \frac{dZ}{dW}$$

Example – Inverse von Bertalanffy Model 4

Solution 2 (cont): The derivative of the **Inverse von Bertalanffy Model** is

$$\frac{da}{dZ} = -52.63\frac{1}{Z}$$

We will show

$$\frac{da}{dW} = \frac{da}{dZ} \times \frac{dZ}{dW}$$

Since $Z = 20.2 - W$ and $\frac{dZ}{dW} = -1$, the formula gives

$$\frac{da}{dW} = \frac{52.63}{20.2 - W}$$

Example – Inverse von Bertalanffy Model 5

Solution 2 (cont): The **Inverse von Bertalanffy Model**

$$a(W) = 158.2 - 52.63\ \ln(20.2 - W)$$

Example – Inverse von Bertalanffy Model 5

Solution 2 (cont): The **Inverse von Bertalanffy Model**

$$a(W) = 158.2 - 52.63\ \ln(20.2 - W)$$

- $a(W)$ has a domain of $W < 20.2$

Example – Inverse von Bertalanffy Model

Solution 2 (cont): The **Inverse von Bertalanffy Model**

$$a(W) = 158.2 - 52.63\ \ln(20.2 - W)$$

- $a(W)$ has a domain of $W < 20.2$
- There is a vertical asymptote at $W = 20.2$

Example – Inverse von Bertalanffy Model 5

Solution 2 (cont): The **Inverse von Bertalanffy Model**

$$a(W) = 158.2 - 52.63\ln(20.2 - W)$$

- $a(W)$ has a domain of $W < 20.2$
- There is a vertical asymptote at $W = 20.2$
- The derivative shows that this function is strictly increasing

Example – Inverse von Bertalanffy Model 5

Solution 2 (cont): The **Inverse von Bertalanffy Model**

$$a(W) = 158.2 - 52.63\ \ln(20.2 - W)$$

- $a(W)$ has a domain of $W < 20.2$
- There is a vertical asymptote at $W = 20.2$
- The derivative shows that this function is strictly increasing
- Since the function W(a) passes through the origin, its inverse function also passes through the origin

$$a(0) = 158.2 - 52.63\ \ln(20.2) = 0$$

Example – Inverse von Bertalanffy Model 5

Solution 2 (cont): Graphing the Inverse von Bertalanffy Model