Calculus for the Life Sciences I

Lecture Notes – Product Rule

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Outline

Tumor Growth) 1

Cancer and Tumor Growth: Mathematical Role

- Image Processing
- Calculating therapeutic doses
- Epidemiology of cancer in a population
- Growth of tumors

Tumor Growth 2

Tumor Growth

- Tumors grow based on the nutrient supply available
- **Tumor angiogenesis** is the proliferation of blood vessels that penetrate into the tumor to supply nutrients and oxygen and to remove waste products
- The center of the tumor largely consists of dead cells, called the **necrotic center** of the tumor
- The tumor grows outward in roughly a spherical shell shape

Gompertz Growth Model 1

Gompertz Growth Model

- Laird (1964) showed that tumor growth satisfies Gompertz growth equations:

$$G(N) = N(b - a\ \ln(N))$$

- N is the number of tumor cells
- a and b are constants matched to the data
- This function is not defined for $N = 0$
  - However, can be shown that

$$\lim_{N\to 0} G(N) = 0$$

Gompertz Growth Model 2

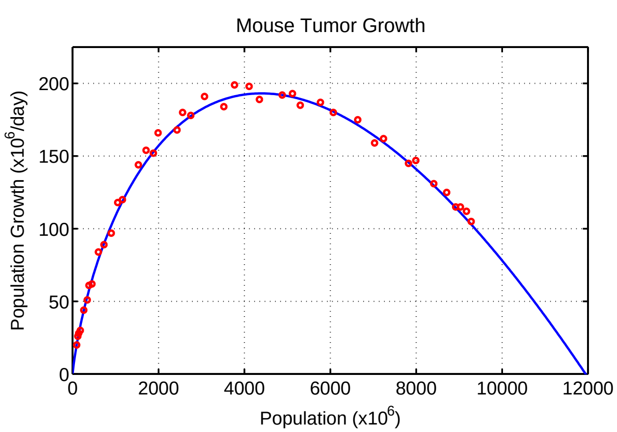
Tumor Growth: Simpson-Herren and Lloyd (1970) studied the growth of tumors

- They studied the C3H Mouse Mammary tumor
- Tritiated thymidine was used to measure the cell cycles
- This gave the growth rate for these tumors

Gompertz Growth Model 3

Mouse Tumor Growth and Gompertz Model: The best fit to the Gompertz Model is

$$G(N) = N(0.4126 - 0.0439\ \ln(N))$$



Gompertz Growth Model 4

Tumor Growth and Gompertz Model:

- The growth of the tumor stops at equilibrium
- The tumor is at its maximum size supportable with the available nutrient supply
- We also want to know when the tumor is growing most rapidly
  - This occurs when the derivative is zero
  - Most cancer therapies attack growing cells
  - Treatment has its maximum effect when maximum growth is occurring

Equilibrium for Gompertz Model

Equilibrium for Gompertz Model: The equilibrium satisfies:

$$G(N) = N(b - a\ \ln(N)) = 0$$

Since $N > 0$, this occurs when $b - a\ \ln(N_e) = 0$ or

$$\begin{aligned} \ln(N_e) &= \frac{b}{a} \\ N_e &= e^{b/a} \end{aligned}$$

This is the unique equilibrium of the **Gompertz Model** or its **carrying capacity**

For the mouse tumor data above

$$N_e = e^{0.4126/0.0439} = e^{9.399} = 12{,}072,$$

which matches the P-intercept on the graph

Maximum Growth from Gompertz Model

Maximum Growth from Gompertz Model: The Gompertz Model is

$$G(N) = N(b - a\ \ln(N))$$

- The graph shows the maximum growth occurs near where the population of tumor cells is about 4,000 ($\times 10^6$)
- Our techniques of Calculus can find the maximum – set the derivative equal to zero
- Finding the derivative of $G(N)$ presents a new problem in differentiation
- We need the **product rule for differentiation** to differentiate $G(N)$

Product Rule

Product Rule: Let $f(x)$ and $g(x)$ be differentiable functions. The product rule for finding the derivative of the product of these two functions is given by:

$$\frac{d}{dx}(f(x)g(x)) = f(x)\frac{dg(x)}{dx} + \frac{df(x)}{dx}g(x)$$

In words, this says that the **derivative of the product of two functions** is the **first function times the derivative of the second function plus the second function times the derivative of the first function**

Product Rule - Example

Product Rule Example: By the **Power rule** we know that if $f(x) = x^5$, then

$$f'(x) = 5x^4$$

Let $f_1(x) = x^2$ and $f_2(x) = x^3$, then $f(x) = f_1(x)f_2(x)$

From the **product rule**

$$\begin{aligned} f'(x) &= f_1(x)f_2'(x) + f_1'(x)f_2(x) \\ &= x^2(3x^2) + (2x)x^3 \ = \ 5x^4 \end{aligned}$$

Example – Product Rule

Example: Consider the function

$$f(x) = (x^3 - 2x)(x^2 + 5)$$

Find the derivative of $f(x)$

Skip Example

Solution: From the **product rule**

$$\begin{aligned} f'(x) &= (x^3 - 2x)(2x) + (x^2 + 5)(3x^2 - 2) \\ &= 2\,x^4 - 4\,x^2 + 3\,x^4 - 2\,x^2 + 15\,x^2 - 10 \\ f'(x) &= 5\,x^4 + 9\,x^2 - 10 \end{aligned}$$

Example – Product Rule

Example: Consider the function

$$g(x) = (x^2 + 4)\ln(x)$$

Find the derivative of $g(x)$

Skip Example

Solution: From the **product rule**

$$\begin{aligned} g'(x) &= (x^2 + 4)\frac{1}{x} + (\ln(x))(2x) \\ g'(x) &= x + \frac{4}{x} + 2x\,\ln(x) \end{aligned}$$

Maximum Growth for the Gompertz Tumor Growth Model 1

Maximum Growth for the Gompertz Tumor Growth Model:
Apply the Product Rule to the Gompertz Growth function

$$G(N) = N(b - a\,\ln(N))$$

The **derivative** is

$$\begin{aligned} \frac{dG}{dN} &= N\left(-\frac{a}{N}\right) + (b - a\,\ln(N)) \\ \frac{dG}{dN} &= (b - a) - a\,\ln(N) \end{aligned}$$

Maximum Growth for the Gompertz Tumor Growth Model 2

Maximum Growth for the Gompertz Tumor Growth Model:
The maximum occurs when $G'(N) = 0$ or

$$a\,\ln(N_{max}) = b - a \quad \text{and} \quad N_{max} = e^{(b/a-1)}$$

Applied to the Gompertz model for the mouse mammary tumor, then the maximum occurs at the population

$$N_{max} = e^{(9.399-1)} = 4,441(\times 10^6)$$

Substituted into the Gompertz growth function, the maximum growth of mouse mammary tumor cells is

$$G(N_{max}) = 4441(0.4126 - 0.0439\,\ln(4441)) = 195.0(\times 10^6/\text{day})$$

Ricker Function 1

Example – Ricker Function: Consider the Ricker function

$$R(x) = 5x\,e^{-0.1x}$$

The function is used in modeling populations.

- Find intercepts
- Find all extrema
- Find points of inflection
- Sketch the graph

Ricker Function 2

Solution: For the Ricker function

$$R(x) = 5x\,e^{-0.1x}$$

The only intercept is the origin, **(0, 0)**

By the **product rule**, the derivative is

$$\frac{dR}{dx} = 5x(-0.1\,e^{-0.1x}) + 5\,e^{-0.1x} = 5\,e^{-0.1x}(1 - 0.1\,x)$$

Since the exponential is never zero, the only **critical point** satisfies

$$1 - 0.1\,x = 0 \quad \text{or} \quad x = 10$$

There is a maximum at

$$(10, 50\,e^{-1}) \quad \text{or} \quad (10, 18.4)$$

Ricker Function 3

Solution (cont): The derivative of the Ricker function is

$$\frac{dR}{dx} = 5\,e^{-0.1x}(1 - 0.1\,x)$$

The second derivative of the Ricker function is

$$\frac{d^2R}{dx^2} = 5\,e^{-0.1x}(-0.1) + 5(-0.1)e^{-0.1x}(1 - 0.1x) = 0.5\,e^{-0.1x}(0.1\,x - 2)$$

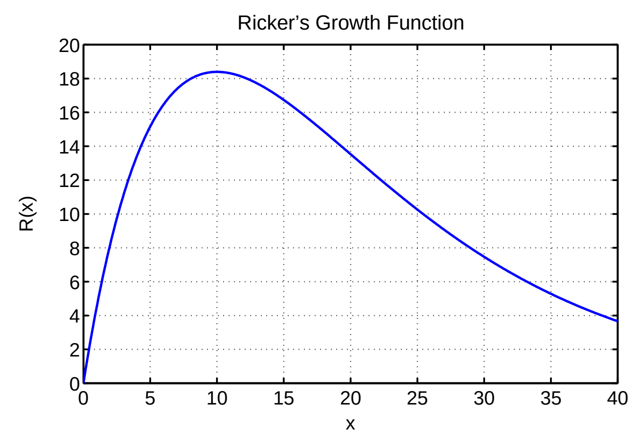
- The point of inflection is found by solving $R''(x) = 0$
- The point of inflection occurs at $x = 20$

$$(20, 100\,e^{-2}) \quad \text{or} \quad (20, 13.5)$$

Ricker Function 4

Solution (cont): Graph of the Ricker function

$$R(x) = 5x\,e^{0.1x}$$



Example – Graphing 1

Example: Consider the function

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

Skip Example

- Determine the domain of the function
- Find any intercepts
- Find critical points and extrema
- Sketch the graph of $f(x)$ for $0 < x \leq 2$

Example – Graphing 2

Solution: For $f(x) = x\ \ln(x)$

- The domain of the function is $x > 0$
- There is no y-intercept
- It can be shown
$$\lim_{x \to 0^+} f(x) = 0$$
- The x-intercept is found by solving $f(x) = 0$, which gives $x = 1$

Example – Graphing 3

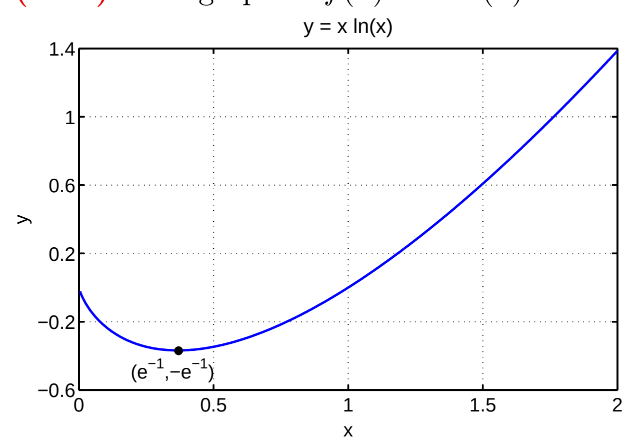
Solution (cont): For $f(x) = x\ \ln(x)$ by the product rule the derivative is

$$f'(x) = x\left(\frac{1}{x}\right) + \ln(x) = 1 + \ln(x)$$

- The **critical point** satisfies
$$1 + \ln(x_c) = 0$$
- Thus, the critical value of x_c satisfies
$$\ln(x_c) = -1 \quad \text{or} \quad x_c = e^{-1} \approx 0.3679$$
- The function value at the critical point is
$$f(e^{-1}) = -e^{-1} \approx -0.3679$$
- There is a **minimum** on the graph at $(e^{-1}, -e^{-1})$

Example – Graphing 4

Solution (cont): The graph of $f(x) = x\ \ln(x)$ is



Example – Graphing 1

Example: Consider the function

$$f(x) = (2 - x)e^x$$

Skip Example

- Find any intercepts
- Find any asymptotes
- Find critical points and extrema
- Sketch the graph of $f(x)$

Example – Graphing 2

Solution: For $f(x) = (2 - x)e^x$

- Since $f(0) = 2$, the y-intercept is $(0, 2)$
- Since the exponential function is never zero, the x-intercept is $(2, 0)$
- It can be shown

$$\lim_{x \to -\infty} f(x) = 0$$

  - An exponential function dominates any polynomial function
  - $f(x)$ goes to 0, so there is a **horizontal asymptote** to the left at $y = 0$

Example – Graphing 3

Solution (cont): For $f(x) = (2 - x)e^x$ by the product rule the derivative is

$$f'(x) = (2 - x)e^x + (-1)e^x = (1 - x)e^x$$

- The **critical point** satisfies

$$(1 - x_c)e^{x_c} = 0$$

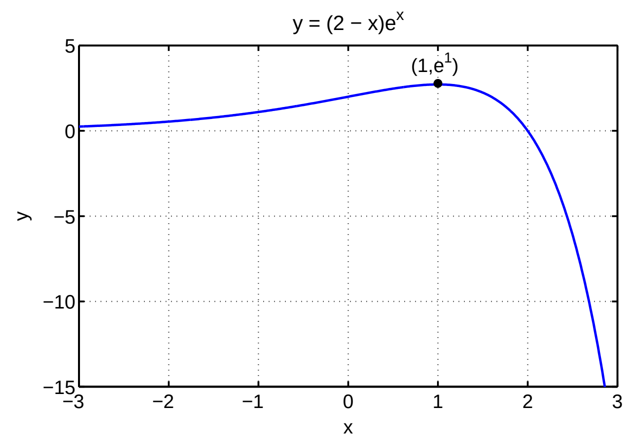
- The critical value is $x_c = 1$
- The function value at the critical point is

$$f(1) = e^1 \approx 2.718$$

- There is a **maximum** on the graph at $(1, e^1)$

Example – Graphing 4

Solution (cont): The graph of $f(x) = (2 - x)e^x$ is



Example – Growth of Tumor 1

Example: Suppose the growth of a tumor satisfies Gompertz growth function

$$G(W) = W(0.5 - 0.05\ \ln(W)),$$

where W is the weight of the tumor in mg

- Find the equilibrium weight of the tumor
- Find the maximum growth rate for this tumor
- Sketch the graph of $G(W)$

Example – Growth of Tumor 2

Solution: The **equilibrium** is found by solving $G(W)$ equal to zero

$$\begin{aligned} G(W) &= W(0.5 - 0.05\ \ln(W)) = 0 \\ 0.5 - 0.05\ \ln(W) &= 0 \\ \ln(W) &= 10 \\ W &= e^{10} = 22,026 \text{ mg} \end{aligned}$$

Example – Growth of Tumor 3

Solution cont): The **maximum growth** is found by setting the derivative $G'(W) = 0$

$$\begin{aligned} G'(W) &= W\left(-\frac{0.05}{W}\right) + (0.5 - 0.05\ \ln(W)) \\ G'(W) &= 0.45 - 0.05\ \ln(W) = 0 \\ \ln(W) &= 9 \\ W &= e^{9} = 8,103 \text{ mg} \end{aligned}$$

The maximum growth rate

$$G(8,103) = 8,103(0.5 - 0.05\ \ln(8,103)) = 405.2 \text{ mg/day}$$

Example – Growth of Tumor 4

Solution (cont): The graph of

$$G(W) = W(0.5 - 0.05\ \ln(W)),$$