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Mercury in Fish
Lead Build Up in Children

### Calculus for the Life Sciences

Lecture Notes – Differential Equations and Integration

Department of Mathematics and Statistics
Dynamical Systems Group
Computational Sciences Research Center
San Diego State University
San Diego, CA 92182-7720

 $http://www-rohan.sdsu.edu/{\sim}jmahaffy$ 

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### Outline



#### Introduction



- Background
- Newton's law of motion
- Differential Equation
- Velocity of Cat
- Height of Cat



#### Differential Equation with Only Time Varying Function

#### Antiderivatives and Integrals

- Basic Integrals
- Linearity of Integrals
- Integral Examples
- Differential Equation Examples
- Height of a Ball



- Introduction
- Modeling Mercury in Fish
- 6 Lead Build Up in Children



### Introduction

#### Introduction

- Begin the study of antiderivatives or integrals
- Previously, studied differential equations that vary linearly with the unknown function (dependent variable)
  - Malthusian growth
  - Radioactive decay
  - Newton's law of cooling
  - Contamination of a lake
- Time varying (the independent variable) terms entering the equation require other techniques
  - Objects under the influence of gravity
  - Time varying buildup of contaminants in an animal





#### Falling Cat

- The cat has evolved to be a stealthy animal with quick reflexes and extremely good jumping ability
- Members of the cat family are considered the best mammalian predators on this planet, occupying a very wide range of niches
- Many of the smaller cats have adapted to hunting in trees (or perhaps larger cats have adapted to ground hunting)
- Cats evolved a very flexible spine, which aids in their ability to spring for prey, absorb shock from their lightning fast strikes, and rapidly rotate their bodies in mid air
- With their very sensitive inner ear for balance, which is combined with quick reflexes and a flexible spine, a cat that falls is capable of righting itself very rapidly, insuring that it lands on the ground feet first



### Falling Cat - Scientific Studies

- This property of falling feet first has been admired by humans for many years
- There was a study in the Annals of Improbable Research (1998) on the number of times a particular cat ended up on its feet when dropped from several different heights
- There was a scientific study of cats falling out of New York apartments, where paradoxically the cats falling from the highest apartments actually fared better than ones falling from an intermediate height
- [1] Jared M. Diamond (1988), Why cats have nine lives, Nature 332, pp 586-7





To the left is the dynamics of a cat falling from an inverted position and ending on its feet

It has been shown that a cat can react sufficiently fast that this inversion process (which itself has been the subject of detailed studies) can happen in about 0.3 seconds

With this information, determine the minimum height from which a cat can be dropped to insure that it lands on its feet

### Model for the Falling Cat

- The physics of the cat rotating during a fall is a moderately complex study
- Our problem is to find if the cat has sufficient time to right itself
- Use Newton's law of motion
  - Mass times acceleration is equal to the sum of all the forces acting on the object
- Since the cat is falling only a short distance at a fairly low velocity, it is safe to assume that the only force acting on the cat is gravity



### Falling Cat

Model for the Falling Cat Newton's law of motion

• Equation for Falling Cat

$$ma = -mg$$

- m is the mass of the cat
- a is the acceleration of the cat
- $\bullet$  -mg is the force of gravity (assuming up is positive)
- q is a constant  $(q = 979 \text{ cm/sec}^2 \text{ at a latitude like San})$ Diego when you add centripetal acceleration to the standard value given for g, which is 980.7 cm/sec<sup>2</sup>)



### Falling Cat

### Differential Equation

- Recall that acceleration is the derivative of the velocity
- Velocity is the derivative of position
- Let h(t) be the height (or position) of the cat at any time t
- The equation above implies that the height of a cat is governed by the differential equation

$$\frac{d^2h}{dt^2} = -g$$

• This is a second order linear differential equation



### Differential Equation (cont)

- The height of the cat is found by solving this differential equation with two initial conditions
- Since the cat is simply falling, assume that the initial velocity starts from rest, so is zero

$$v(0) = h'(0) = 0$$

• Let ground level be a height of zero, so the cat begins at some height above ground level,

$$h(0) = h_0 > 0$$

• The problem reduces to solving this initial value problem and finding what values  $h_0$  of produce a solution such that



### Solution - Velocity of Cat

- Acceleration is the derivative of velocity, so find the velocity at any time
- Thus, solve the first order differential equation

$$v'(t) = -g \quad \text{with} \quad v(0) = 0$$

- What velocity function v(t), which upon differentiation produces -q, a constant?
- We need an **antiderivative** of a constant
- The derivative of a straight line produces a constant
- A straight line with a slope of -g is

$$v(t) = -gt + c$$



Solution (cont) - Velocity of Cat: The velocity satisfies

$$v(t) = -gt + c$$

- Notice that the antiderivative produces an arbitrary constant, since the derivative of any constant is zero
- The initial conditions find the arbitrary constant

$$v(0) = c = 0$$

• The velocity for any time is

$$v(t) = -gt$$



### Falling Cat

**Solution - Height of Cat:** The velocity is the derivative of the height

- Find an antiderivative of velocity to determine the height of the cat
- Solve the initial value problem

$$h'(t) = v(t) = -gt$$
 with  $h(0) = h_0$ 

- We must find an antiderivative of -qt
- Recall that a quadratic function has a linear derivative
- The general solution of this initial value problem is

$$h(t) = -\frac{gt^2}{2} + c$$
 c arbitrary



### Falling Cat

### Solution (cont) - Height of Cat:

- The initial condition gives  $h(0) = h_0 = c$
- The height of the cat any time t satisfies

$$h(t) = -\frac{gt^2}{2} + h_0$$

• With  $g = 979 \text{ cm/sec}^2$ , the equation for height in centimeters is

$$h(t) = h_0 - 489.5 t^2$$

• Evaluate this at t = 0.3 sec and obtain

$$h(0.3) = h_0 - 489.5(0.3)^2 = h_0 - 44.055 \text{ cm}$$

• Thus, the cat must be higher than 44.1 cm for it to have sufficient time to right itself before hitting the ground (This is about 1.5 feet)



# Differential Equation with Only Time Varying Function

### Differential Equation with Only Time Varying Function

- There is a special class of differential equations where the derivative of the unknown function depends only on a time varying function f(t) (no dependence on y)
- These differential equations satisfy

$$\frac{dy}{dt} = f(t)$$

- The solution to this differential equation is an antiderivative of the function f(t)
- The antiderivative is also known as the **integral**
- The solution of the time varying differential equation is written

$$y(t) = \int f(t) \, dt$$



### Antiderivatives and Integrals

### Antiderivatives and Integrals

- A function F(t) is an antiderivative of f(t) if F'(t) = f(t)
- From the formula for the derivative of  $t^{n+1}$ , we see that

$$\frac{d}{dt}(t^{n+1}) = (n+1)t^n$$

• The antiderivative satisfies

$$(n+1) \int t^n dt = t^{n+1}$$

• The integral formula for  $t^n$  can be written

$$\int t^n dt = \frac{t^{n+1}}{n+1} + C$$

• Note that the integral formula has an arbitrary constant CSDSU

### Antiderivatives and Integrals

### **Antiderivatives and Integrals**

• The integral of a constant is a linear function

$$\int k \, dt = k \, t + C$$

• Other Basic Integrals

$$\int e^{kt}dt = \frac{e^{kt}}{k} + C$$

$$\int \frac{dt}{t} = \ln|t| + C$$

$$\int \cos(kt)dt = \frac{\sin(kt)}{k} + C$$

$$\int \sin(kt)dt = -\frac{\cos(kt)}{k} + C$$



# Antiderivatives and Integrals

**Linearity of Integrals** Let F(t) and G(t) be antiderivatives of f(t) and g(t) and constants k and C

• Additive Property:

$$\int (f(t) + g(t))dt = \int f(t)dt + \int g(t)dt = F(t) + G(t) + C$$

• Scalar Property:

$$\int k f(t)dt = k \int f(t)dt = k F(t) + C$$



### **Example 1:** Consider the integral

$$\int \left(2x^3 - e^{-5x} + \frac{2}{x^2}\right) dx$$

Skip Example

$$\int \left(2x^3 - e^{-5x} + \frac{2}{x^2}\right) dx = 2\left(\frac{x^4}{4}\right) - \left(\frac{e^{-5x}}{-5}\right) + \int 2x^{-2} dx$$
$$= \frac{x^4}{2} + \frac{e^{-5x}}{5} + \left(\frac{2x^{-1}}{-1}\right) + C$$
$$= \frac{x^4}{2} + \frac{e^{-5x}}{5} - \frac{2}{x} + C$$



### **Example 2:** Consider the integral

$$\int \left(4\sin(2x) - \frac{3}{x}\right) dx$$

Skip Example

$$\int \left(4\sin(2x) - \frac{3}{x}\right) dx = 4\left(\frac{-\cos(2x)}{2}\right) - 3\ln(x) + C$$
$$= -2\cos(2x) - 3\ln(x) + C$$



### **Example 3:** Consider the integral

$$\int \left(3x^2 - 4e^{-x}\right)dx$$

Skip Example

$$\int (3x^2 - 4e^{-x}) dx = 3\left(\frac{x^3}{3}\right) - 4(-e^{-x}) + C$$
$$= x^3 + 4e^{-x} + C$$



**Example 4:** Consider the integral

$$\int \left(2\sin(3x) - \frac{4}{x^3}\right) dx$$

Skip Example

$$\int \left(2\sin(3x) - \frac{4}{x^3}\right) dx = 2\left(\frac{-\cos(3x)}{3}\right) - 4\int x^{-3} dx$$
$$= -\frac{2}{3}\cos(3x) - 4\frac{x^{-2}}{-2} + C$$
$$= -\frac{2}{3}\cos(3x) + \frac{2}{x^2} + C$$



### **Example 5:** Consider the integral

$$\int \left(3\cos\left(\frac{t}{2}\right) - \frac{1}{2t}\right)dt$$

Skip Example

$$\int \left(3\cos\left(\frac{t}{2}\right) - \frac{1}{2t}\right)dt = 3\left(\frac{\sin\left(\frac{t}{2}\right)}{\frac{1}{2}}\right) - \frac{1}{2}\ln(t) + C$$
$$= 6\sin\left(\frac{t}{2}\right) - \frac{1}{2}\ln(t) + C$$



### **Example 6:** Consider the integral

$$\int \left(6\sqrt{t} - e^{2t} - 3\right) dt$$

Skip Example

$$\int \left(6t^{1/2} - e^{2t} - 3\right) dt = 6\left(\frac{t^{3/2}}{\frac{3}{2}}\right) - \frac{e^{2t}}{2} - 3t + C$$
$$= 4t^{3/2} - \frac{1}{2}e^{2t} - 3t + C$$



### **DE Example 1:** Initial Value Problem

$$\frac{dy}{dt} = 4t - e^{-2t}, \qquad y(0) = 10$$

Skip Example

$$y(t) = \int (4t - e^{-2t}) dt = 2t^2 + \frac{1}{2}e^{-2t} + C$$

$$y(0) = \frac{1}{2} + C = 10$$
 so  $C = \frac{19}{2}$ 

$$y(t) = 2t^2 + \frac{1}{2}e^{-2t} + \frac{19}{2}$$



### **DE Example 2:** Initial Value Problem

$$\frac{dy}{dt} = 2t - \sin(t), \qquad y(0) = 3$$

Skip Example

$$y(t) = \int (2t - \sin(t)) dt = t^2 + \cos(t) + C$$

$$y(0) = 1 + C = 3$$
 so  $C = 2$ 

$$y(t) = t^2 + \cos(t) + 2$$



### **DE Example 3:** Initial Value Problem

$$\frac{dy}{dt} = 4 - 2y, \qquad y(0) = 5$$

Skip Example

**Solution:** Rewrite y' = -2(y-2), so this linear differential equation

Make substitution 
$$z(t) = y(t) - 2$$
, so  $z(0) = 5 - 2 = 3$ 

$$\frac{dz}{dt} = -2z, \text{ with } z(0) = 3$$

$$z(t) = 3e^{-2t} = y(t) - 2$$
 or  $y(t) = 2 + 3e^{-2t}$ 



### **DE Example 4:** Initial Value Problem

$$\frac{dy}{dt} = \frac{4}{t}, \qquad y(1) = 2$$

Skip Example

$$y(t) = \int \left(\frac{4}{t}\right) dt = 4\ln(t) + C$$

$$y(1) = 4\ln(1) + C = 2$$
 so  $C = 2$ 

$$y(t) = 4\ln(t) + 2$$



1

**Height of a Ball:** A ball is thrown vertically with gravity  $(g = 32 \text{ ft/sec}^2)$  being the only force acting on the ball (air resistence is ignored)

- Assume that the ball begins at ground level, h(0) = 0 ft, and is given an initial upward velocity of 64 ft/sec (about 44 mph)
- Determine the height of the ball, h(t), at any time  $t \ge 0$ , and when the ball hits the ground
- Find the maximum height of the ball and the velocity with which it hits the ground
- Graph the solution for all time up until the ball hits the ground



Solution: Newton's law of motion with the mass of the ball, m, acceleration of the ball, a, and force of gravity, mg, satisfies

$$ma = -mg$$
 or  $a = -g = -32$ 

• Acceleration is the derivative of velocity, so

$$a = \frac{dv}{dt} = -32$$

• Thus,

$$v(t) = -\int 32 \, dt = -32 \, t + C$$

• The initial velocity is v(0) = 64 ft/sec, so

$$v(0) = C = 64$$
 or  $v(t) = 64 - 32t$ 



### Solution (cont): Velocity Equation satisfies

$$v(t) = 64 - 32t$$

• Velocity is the derivative of position or height, h(t)

$$v(t) = \frac{dh}{dt} = 64 - 32t$$

• Thus,

$$h(t) = \int (64 - g t)dt = 64t - 16t^2 + C_1$$

• The initial height is  $h(0) = C_1 = 0$  ft, so

$$h(t) = 64 \, t - 16 \, t^2$$



### Solution (cont): Height Equation is

$$h(t) = 64t - 16t^2 = -16t(t-4)$$

• The ball hits the ground at t=4 sec with

$$v(4) = 64 - 32(4) = -64$$
 ft/sec

• At the **maximum height**, the velocity is zero

$$v(t) = 64 - 32t = 0$$
 or  $t = 2 \sec t$ 

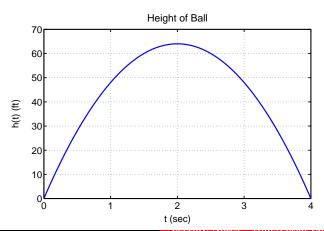
• The maximum height is

$$h(2) = 64(2) - 16(4) = 64$$
 ft



Joseph M. Mahaffy, (jmahaffy@mail.sdsu.edu)

### Graph of Height of the Ball





### Introduction - Fish in the Great Lakes Region

- Fishing is an important recreational activity around the Great Lakes
- Since the mid-1970s, the Michigan Department of Health has been issuing warnings about eating the fish from the Great Lakes
- The greatest concern is the buildup of PCBs in fatty tissues
  - PCBs are linked to cancer
  - PCBs have estrogen effects that might disrupt development
  - PCBs have declined 90% since 1975



### Introduction - Mercury in the Great Lakes Region

- Mercury (Hg) is concentrated in the tissues of the fish
- Mercury, a heavy metal, is a dangerous neurotoxin that is very difficult to remove from the body
- It concentrates in the tissues of fish, particularly large predatory fish such as Northern Pike, Lake Trout, Bass, and Walleye
- The primary sources of mercury in the Great Lakes region
  - Runoff of different minerals that are mined
    - Incinerators that burn waste, especially batteries
    - Most batteries no longer contain mercury
- Bacteria converts mercury into the highly soluble methyl mercury
  - Enters fish by simply passing over their gills
  - Larger fish consume small fish and concentrate mercury



#### Introduction - Mercury and Health

- Higher levels of Hg in fish may cause children problems in their developing neural system
- Mercury in the diet may lead to impaired development of the nervous system and learning disorders
- There is a warning that young children and pregnant women should limit their consumption to less than one fish per month and avoid the larger, fattier, predatory fishes with some fish caught in certain areas to be avoided all together
- The fat problem is for the PCBs, not the Hg
- Others are recommended to limit their consumption to less than one fish a week and avoid eating the larger fish, such as Lake Trout over 22 inches



### Mercury in Fish

#### Introduction - Mercury Buildup in Fish

- So why do fish build up the dangerous levels of Hg in their tissues?
- Hg is not easily removed from the system, so when ingested it tends to remain in the body
- The best way to remove heavy metals is the use of chelating agents
- Mathematically, this build up is seen as the integral of the ingested Hg over the lifetime of the fish
- Thus, older and larger fish should have more Hg than the younger fish



#### Modeling Mercury in Fish - Model Weight of a Fish

- Classic model for growth of a fish (length) is the **von** Bertalanffy equation
- The record Lake Trout in Michigan is 27.9 kg (124 cm in length)
- Assume that the weight of a Lake Trout satisfies the differential equation:

$$\frac{dw}{dt} = 0.015(25 - w)$$
 with  $w(0) = 0$ 

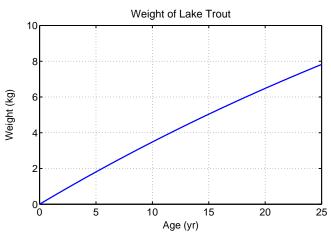
• This is a Linear Differential Equation with the solution:

$$w(t) = 25 - 25 e^{-0.015t}$$

• It takes 5.5 years to reach 2 kg, about 15 years to reach 5 kg, with a limiting level of 25 kg for Lake Trout



### Graph for Weight of Lake Trout





### Modeling Mercury in Fish - Model for Mercury in a Fish

- Assume fish eat food roughly proportional to its weight
- Let H(t) be the amount of Hg (in mg) in a growing Lake Trout
- Assume the concentration of Hg in a fish's food is constant (though in fact, the larger fish will eat more heavily contaminated, larger fish)
- The rate of Hg added to the tissues of a fish satisfies the differential equation with k = 0.03 mg/yr:

$$\frac{dH}{dt} = k \left(25 - 25 e^{-0.015t}\right)$$
 with  $H(0) = 0$ 



Model for Mercury in Fish: The differential equation is

$$\frac{dH}{dt} = k \left(25 - 25 e^{-0.015t}\right)$$
 with  $H(0) = 0$ 

• The right hand side of the differential equation is a function of t only, so solution is found by integrating:

$$H(t) = k \int (25 - 25 e^{-0.015t}) dt$$

• Taking antiderivatives:

$$H(t) = 25k \left( t - \frac{e^{-0.015t}}{-0.015} + C \right)$$



Model for Mercury in Fish: The solution is

$$H(t) = 25k \left( t - \frac{e^{-0.015t}}{-0.015} + C \right)$$

• The initial condition gives H(0) = 0, so

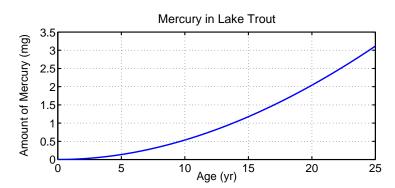
$$H(0) = 25k \left(0 + \frac{200}{3} + C\right)$$
 or  $C = -\frac{200}{3}$ 

• With k = 0.03, the solution becomes

$$H(t) = 0.25(3t + 200e^{-0.015t} - 200)$$
 mg of Hg



### Graph for Mercury in Lake Trout





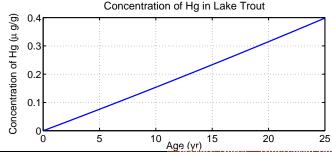
Model for Mercury in Fish: Model gives the amount of Hg in a trout

- The amount of mercury in an aging Lake Trout increases as it eats more prey containing mercury
- It is more important to know what the concentration of mercury in the flesh of the Lake Trout that is eaten
- The concentration of mercury increases in a Lake Trout as it ages
- It is clear why the Michigan Department of Health advises against eating larger fish



Concentration of Mercury in Lake Trout The concentration of Hg is measured in  $\mu$ g (of mercury) per gram (of fish)

$$c(t) = \frac{H(t)}{w(t)}$$





### Lead Build Up in Children: Introduction

- For many years, lead (Pb) was an additive to paint used to reduce molds and improve adhesion
- The federal government required leaded paint be used in low income housing until the late 1960s
- As leaded paint is shed or removed, lead enters dust in homes, reaching levels of 0.5% by weight of lead
- Lead-laden dust is particularly problematic in the development of small children
- They are exposed to lead from the dust ingested by normal hand-to-mouth play activities (crawling followed by thumb-sucking or playing with toys and sucking on them)



#### Lead Build Up in Children: Neural Effects

- The highest exposure to lead is relatively short, but it is a critical time in neural development
- The heavy metals do not leave the body and are often not discovered until after the child enters school at age 5 and is found to have neurological difficulties
- The long term effects of lead in a child can be severe
  - Learning disabilities, decreased growth, hyperactivity, impaired hearing, and even brain damage
  - Concentrations as low as 10  $\mu$ g/dl in the blood results in developmental toxicity (EPA limit dropped to 5  $\mu$ g/dl in 2012)
  - Nerve conduction slows at 20  $\mu$ g/dl in the blood
  - Vitamin D metabolism and hemoglobin synthesis is impaired at 40  $\mu$ g/dl in the blood



### Modeling Lead Build Up in Children

- Multiple pharmacokinetic models have been developed
- Create a model of lead exposure based on a child's activity level
- Assume that the majority of the lead enters through the ingestion of contaminated dirt
- The amount of lead ingested depends on the hand-to-mouth activity of the child
- This activity usually increases from birth to age 2 years, then rapidly declines as other forms of activity replace the hand-to-mouth activities



### Modeling Activity in a Small Girl

• Assume that the hand-to-mouth activity of a small girl in the age 0-24 months satisfies the differential equation

$$\frac{da}{dt} = 0.02(12 - a)$$
 with  $a(0) = 0$ 

- $\bullet$  a(t) is the activity time in hours per day, and t is the age in months
- Solve this differential equation
- Graph the solution
- Determine the activity level in hours per day at age 24 months



Solution for Model of Activity in a Small Girl The differential equation is written:

$$\frac{da}{dt} = -0.02(a - 12)$$
 with  $a(0) = 0$ 

- The differential equation describing the activity of a child, a(t), is very similar to our study of Newton's law of cooling
- Make the substitution, z(t) = a(t) 12, with z'(t) = a'(t), so

$$\frac{dz}{dt} = -0.02z$$
 with  $z(0) = a(0) - 12 = -12$ 

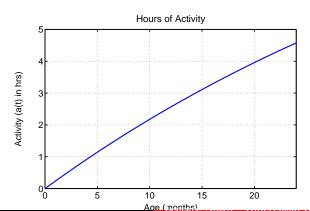
• The solution is  $z(t) = -12 e^{-0.02t} = a(t) - 12$  or

$$a(t) = 12(1 - e^{-0.02t})$$



Graph of Baby Activity: Note that

$$a(24) = 12(1 - e^{-0.48}) = 4.57 \text{ hr}$$





Lead Accumulation in the Child The lead will enter the girl's body proportional to her activity time

$$a(t) = 12(1 - e^{-0.02t})$$

- Bioavailable lead is typically 0.1% of household dust by weight
- Assume the total amount of lead (P(t)) in her body satisfies the differential equation:

$$\frac{dP(t)}{dt} = ka(t) \quad \text{with} \quad P(0) = 0$$

- a(t) is the activity time and  $k = 200 \mu \text{g-day/hour}$  of play/month
- Find the solution P(t) and graph this solution



Solution: Lead Accumulation in the Child The model satisfies P(0) = 0 with

$$\frac{dP}{dt} = 200(12(1 - e^{-0.02t})) = 2400(1 - e^{-0.02t})$$

- The right hand side of this differential equation only depends on t
- Integration of this differential equation gives the solution
- Integration is representative of the accumulation or sum of the past lead acquired through the playing activity
- Obtain the solution from

$$P(t) = 2400 \int (1 - e^{-0.02t}) dt$$



#### Solution: Lead Accumulation in the Child

$$P(t) = 2400 \int (1 - e^{-0.02t}) dt$$

$$= 2400 \left( \int 1 dt - \int e^{-0.02t} dt \right)$$

$$= 2400 \left( t - \frac{e^{-0.02t}}{-0.02} + C \right)$$

$$= 2400 \left( t + 50 e^{-0.02t} + C \right)$$



Solution: Lead Accumulation in the Child The inititial condition is

$$P(0) = 0 = 2400 \left( 0 + 50 e^{-0.02(0)} + C \right)$$

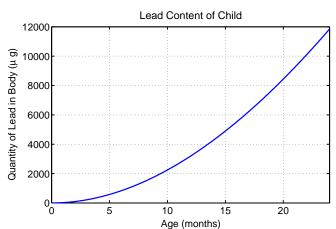
It follows that C = -50 and the solution is

$$P(t) = 2400 \left( t + 50 e^{-0.02t} - 50 \right),$$

where P(t) is measured in  $\mu g$  accumulated by t months



### Graph of Lead Build Up in a Child





Concentration of Lead in the Child: The solution above gives the amount of lead in the girl,

$$P(t) = 2400 \left( t + 50 e^{-0.02t} - 50 \right),\,$$

but it is the concentration that matters

- Assume that this lead is uniformly distributed throughout the body
- Find the lead level measured from blood samples at ages one and two
- Typical measurements are in terms of  $\mu g/dl$
- Note that 10 dl of blood weighs about 1 kg, and a girl at age one (12 months) weighs 10 kg, while she weighs about 12 kg at age 2 (24 months)



**Solution:** Concentration of Lead: From the solution P(t)

$$P(12) = 2400 (12 + 50 e^{-0.24} - 50) = 3195 \mu g,$$

• Since the girl weighs 10 kg, the concentration is given by

$$c(12) = \frac{3195 \ \mu g}{10 \ \text{kg}} = 31.95 \ \mu g/\text{dl}$$

- This value is clearly dangerous to neural development
- A calculation for a girl at age two or 24 months gives

$$P(24) = 2400 (24 + 50 e^{-0.48} - 50) = 11,854 \mu g$$

• Since the girl weighs 12 kg, the concentration is given by

$$c(24) = \frac{11,854 \ \mu g}{12 \ \text{kg}} = 100.5 \ \mu g/\text{dl}$$

• This level is considered deadly

