Applications of logarithmic and exponential functions in Biomedical Science

by

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UCF EXCEL Applications of Calculus

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Calculus Topic: Exponential functions

Topic #1: Logarithmic and Exponential functions

Calculus concept # 1

Exponential functions – review from Calc II

(Iclicker question)

Some of the future courses (that you may take) that this will be relevant:

- MCB 3020 – General Microbiology
- MCB 4414 – Microbial Metabolism
- BCH 4053 – Biochemistry I
- BCH 4054 – Biochemistry II

- **Goals (lecture one):**

  1.) Understand the basics of bacteriology, in particular the cell cycle of a bacterium during logarithmic growth

  2.) Utilize and understand equations that are used to calculate population densities of bacteria in culture

  3.) Gain an appreciation for bacteriology, specifically as it relates to infections and infectious disease states in humans

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- Bacteriology

  Originally termed the study of bacteria, now more generally the study of bacteria (eubacteria), archeabacteria and viruses.

These are all microorganisms. There is still a considerable debate regarding the term 'form of life', specifically as it pertains to viruses and phage.

What do you think???

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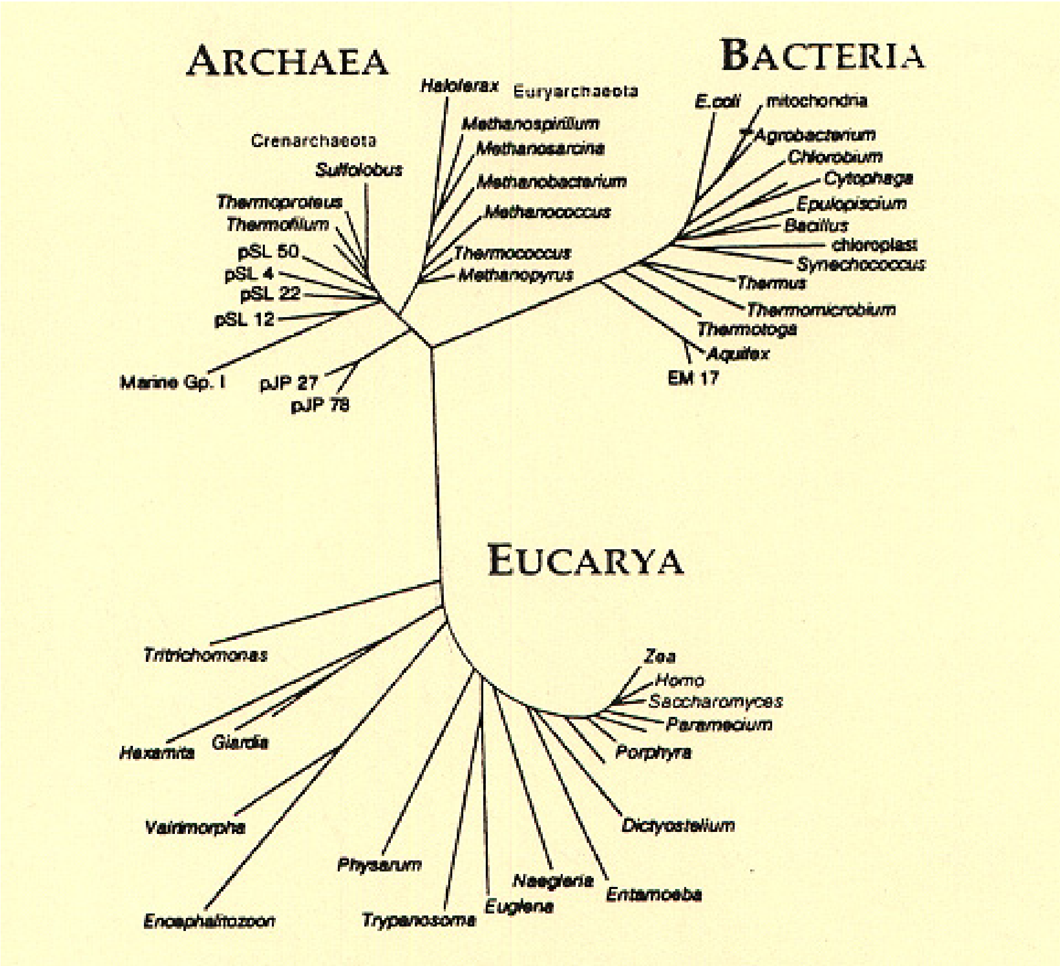

- **Tree of life**

All the way from humans, trees, insects, slime molds, to archaebacteria and bacteria

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- **Infectious diseases**

  Caused by both bacterial and viral **pathogens**

Why do these organisms invade us?

To eat and survive! Most bacterial pathogens have a carbon or nitrogen source they are looking for during their invasion into the host.

How do we know what they are looking for?

In order to study the reason that these bacteria are invading our bodies, we must understand what they like to use as carbon/nitrogen/sulfur sources. This requires the growth of these organisms in test tubes (also called *in vitro*).

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- **Cell cycle of bacteria**

How do we know that certain bacteria prefer certain carbon sources, etc.? We must determine the cell yield and growth rate of bacteria on various carbon sources. This is done best by ‘batch’ growth studies.

Bacteria divide and multiply at a **logarithmic** rate

As such the equations used to determine growth, growth rate and population densities are exponential functions.

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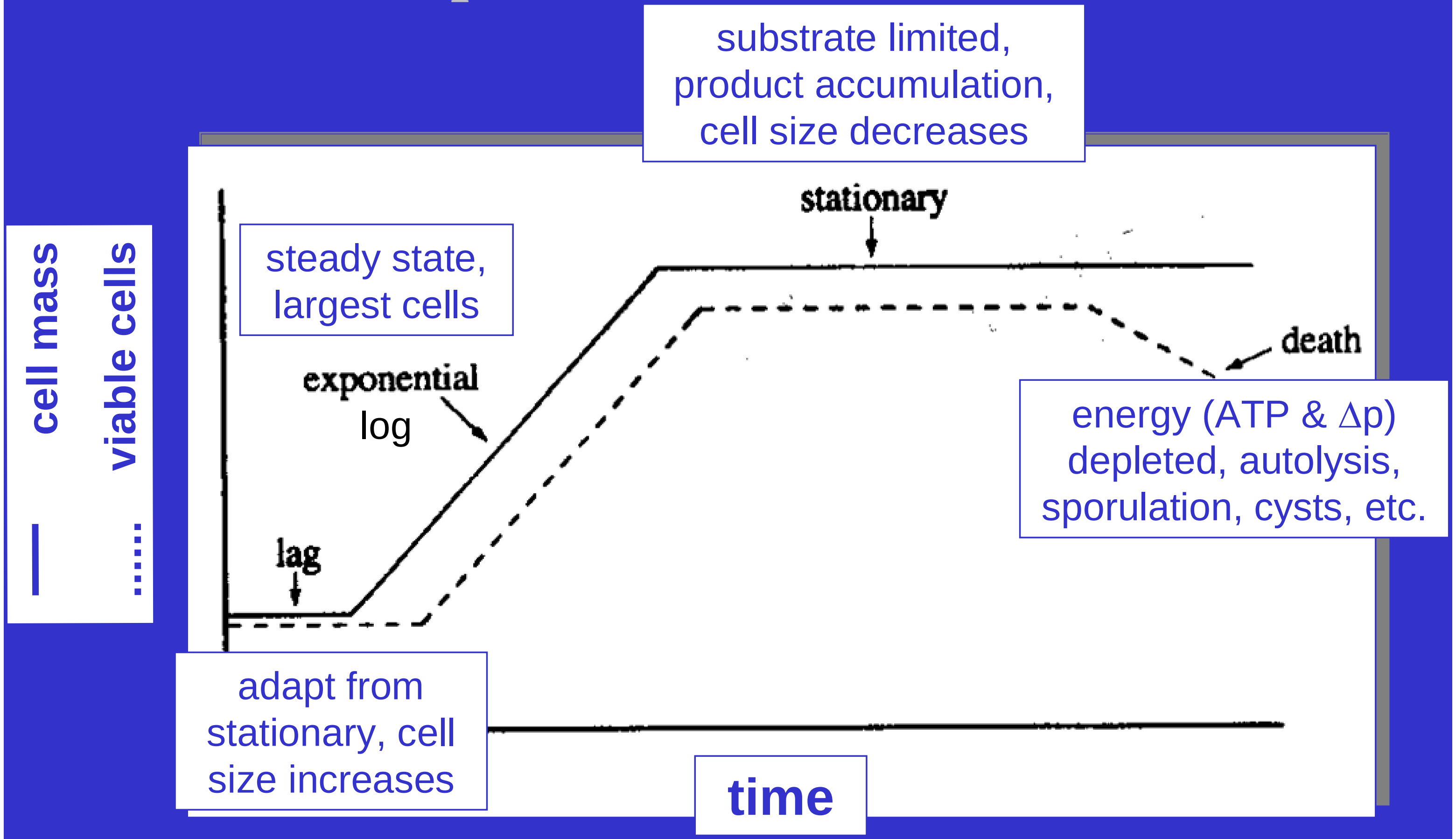
Growth physiology:
Phases of Population Growth



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- There are four phases of growth *(in vitro):*

1) Lag phase
2) Logarithmic phase
3) Stationary phase
4) Death phase

Do these phases occur during growth in the host?

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Lag phase: Cells are adapting to their new environment (after inoculation into fresh medium). They are altering their proteome to best use the nutrients and increasing their size and protein content

Relevance to 'real life' – movement of a bacterium from the gut to the soil, or water supply

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Logarithmic phase: This is the phase at which cells divide rapidly, and their absolute numbers increase in a logarithmic manner. Cells are large, and contain more protein and RNA than slower growth, nutrient limited cells.

Relevance: Once an infection takes root (and is successfully evading the immune response) rapid (logarithmic) growth can ensue

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Stationary phase: As nutrients become limiting (or toxic product inhibit growth), cells reduce in size and produce less protein and RNA per cell. Cells also stop dividing and their growth is not logarithmic.

Relevance: Cells that are limited by a nutrient in the host (e.g. run out of carbon) turn on many stress response proteins during transition to stationary phase

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Death phase: Without removal of a toxic metabolite, or addition of the limiting nutrient, cells will eventually die. Alternatively some cells (such as the pathogen that causes Anthrax) will form a resistant spore that can survive extreme conditions.

Relevance – not much!!! Toxic substances likely do not build up *in situ* in the host during infection, so this part of cell cycle is likely more of an artifact

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- Why study bacteriology?

1.) basic curiosity for nature/**science**

- important for anyone with **STEM** goals

2.) Industrial use (fermentation – **beer and cheese!**)

- originated in public health (how to make drinks potable)

3.) Global **climate changes** (carbon/nitrogen cycles)

- much of the greenhouse gas emissions are from methanogens (soil and ruminants)

4.) **Infectious disease** – each one of us is battling pathogens at this very moment!!!

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- **Infectious disease**

  Infection – an actively growing microorganism (bacterium, virus, fungi, protozoan, parasite) within a host

  Disease – clinically evident illness

Some are communicable – some are not, but all have an infectious agent, usually referred to as a pathogen

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Pathogens – common *Staphylococcus aureus*

S. aureus is a spherical bacterium (coccus) which on microscopic examination appears in pairs, short chains, or bunched, grape-like clusters. These organisms are Gram-positive. Some strains are capable of producing a highly heat-stable protein **toxin** that causes illness in humans.

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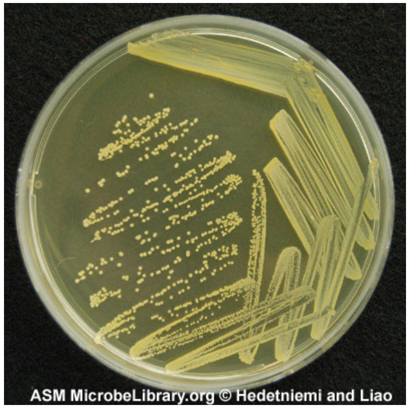
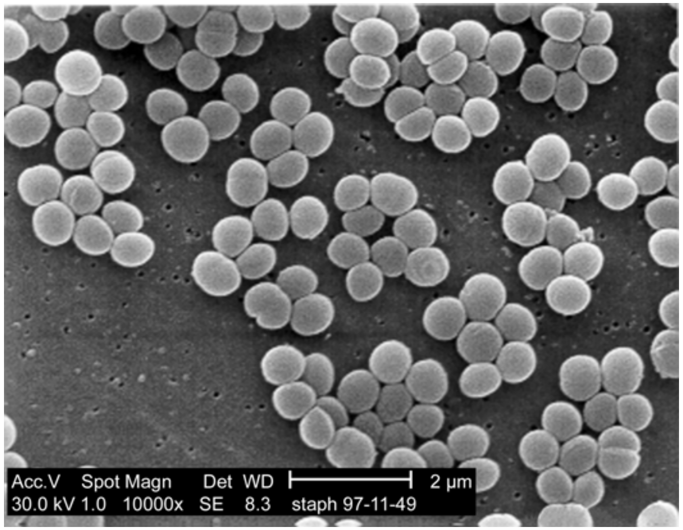
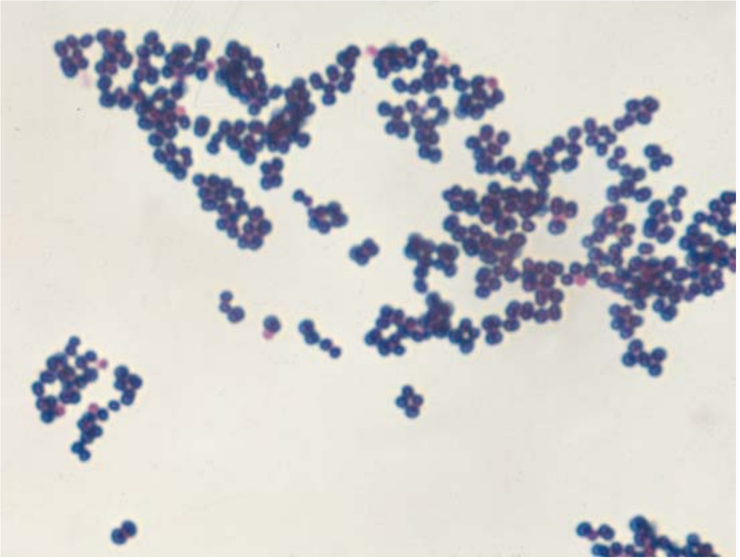
- ***Staphylococcus aureus***



Petri dish

Scanning Electron micrograph





Gram stain

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Salmonella

Salmonella is a rod-shaped, motile bacterium -- nonmotile exceptions *S. gallinarum* and *S. pullorum*--, nonsporeforming and **Gram-negative**. There is a widespread occurrence in animals, especially in poultry and swine.

Environmental sources of the organism include water, soil, insects, factory surfaces, kitchen surfaces, animal feces, raw meats, raw poultry, and raw seafoods, to name only a few.

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Cultured with human cells

Gram (negative) stain

Raw Chicken!!!

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Escherichia coli O157:H7

Currently, there are four recognized classes of **enterovirulent** *E. coli* (collectively referred to as the EEC group) that cause gastroenteritis in humans. Among these is the **enterohemorrhagic** (EHEC) strain designated *E. coli* O157:H7. *E. coli* is a normal inhabitant of the intestines of all animals, including humans.

E. coli serotype O157:H7 is a rare variety of E. coli that produces large quantities of one or more related, potent toxins that cause severe damage to the lining of the intestine. These toxins [verotoxin (VT), shiga-like toxin] are closely related or identical to the toxin produced by *Shigella dysenteriae*.

Infectious dose

The **infectious dose** is the number of bacteria (or virus) that is needed to cause disease in the animal (human). It is clear from the figure above that different types of pathogens can have very different infectious doses. This is due to their variable ability to grow once introduced into host, while attempting to overcome the host's defense mechanisms.

Once inside the host, infections can become deadly very quickly if the host's defense does not eliminate the pathogen. This is due to the rapid logarithmic growth of the cells within the host.

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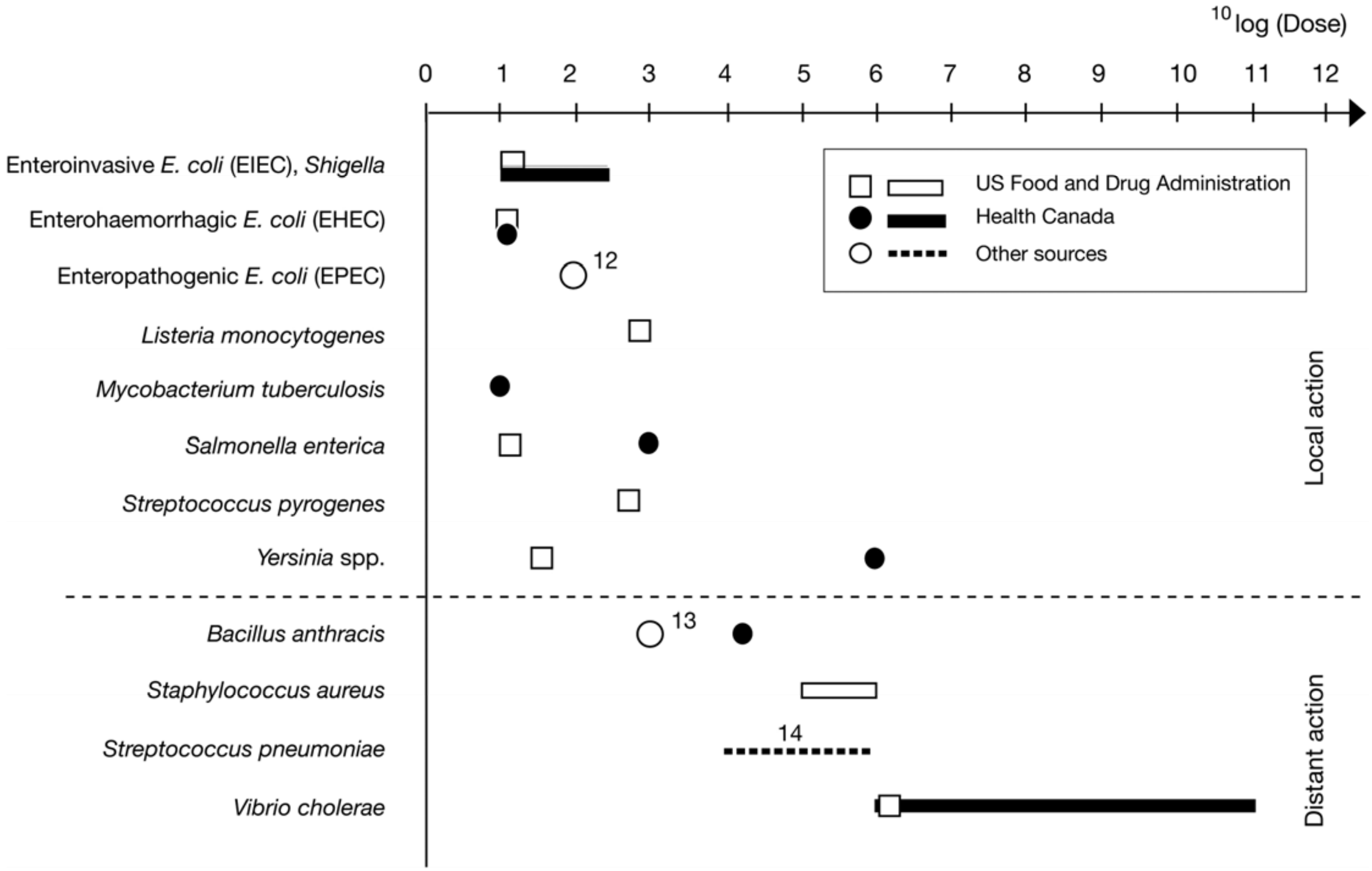

Figure 2. Summary of Infectious doses for several pathogens.

From: Pathogenesis, Virulence, and Infective Dose Schmid-Hempel P, Frank SA PLoS Pathogens Vol. 3, No. 10, e147 doi:10.1371/journal.ppat.0030147

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Calculating growth of bacterial populations

The growth rate of bacterial populations, (assuming they are in the logarithmic phase of growth), is characterized by the following equations:

$$x = x_0 \, 2^y$$

where:

x = anything that doubles each generation

x_0 = starting value

y = number of generations

Definition of Generation time:

The generation time is defined as the time that is required for a population of cells to double in number and can be defined by *g*.

The number of generations can be estimated by dividing the time that has elapsed, *t*, by the generation time *g* as follows:

$$Y = t / g$$

Sample problem:

1.) First, Calculate the number of generations

4 hours time, 20 minute generation time

$Y = t / g$ $\quad$ $Y = 240/20$

$Y = 12$

Sample problem (continued):

If you need a population of 1×10^{10} after 24 hours of growth, what would be the inoculum?

$x = x_0\, 2^{y}$ so $1 \times 10^{10} = x_0\, 2^{12}$

$1 \times 10^{10} / 4096 = x_0$

$X_0 = 2.44 \times 10^{6}$

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