

Curriculum Units by Fellows of the Yale-New Haven Teachers Institute 2009 Volume V: Evolutionary Medicine

Math Morphing Proximate and Evolutionary Mechanisms

Curriculum Unit 09.05.09 by Kenneth William Spinka

Introduction
Background
Essential Questions
Lesson Plans
Website
Student Resources
Glossary Of Terms
Bibliography
Appendix

Introduction

An important theoretical development was Nikolaas Tinbergen's distinction made originally in ethology between evolutionary and proximate mechanisms; Randolph M. Nesse and George C. Williams summarize its relevance to medicine: All biological traits need two kinds of explanation: proximate and evolutionary. The proximate explanation for a disease describes what is wrong in the bodily mechanism of individuals affected

Curriculum Unit 09.05.09 1 of 27

by it. An evolutionary explanation is completely different. Instead of explaining why people are different, it explains why we are all the same in ways that leave us vulnerable to disease. Why do we all have wisdom teeth, an appendix, and cells that if triggered can rampantly multiply out of control? [1]

A fractal is generally "a rough or fragmented geometric shape that can be split into parts, each of which is (at least approximately) a reduced-size copy of the whole," a property called self-similarity. The term was coined by Beno?t Mandelbrot in 1975 and was derived from the Latin fractus meaning "broken" or "fractured." A mathematical fractal is based on an equation that undergoes iteration, a form of feedback based on recursion.

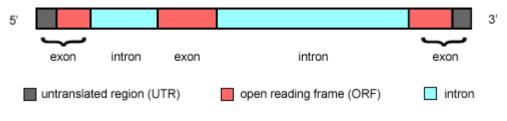
http://www.kwsi.com/ynhti2009/image01.html

A fractal often has the following features:

- 1. It has a fine structure at arbitrarily small scales.
- 2. It is too irregular to be easily described in traditional Euclidean geometric language.
- 3. It is self-similar (at least approximately or stochastically).
- 4. It has a Hausdorff dimension which is greater than its topological dimension (although this requirement is not met by space-filling curves such as the Hilbert curve).
- 5. It has a simple and recursive definition.

Because they appear similar at all levels of magnification, fractals are often considered to be infinitely complex. Natural objects that approximate fractals to a degree include clouds, mountain ranges, lightning bolts, coastlines, and snow flakes however, not all self-similar objects are fractals. For example, the real line, a straight Euclidean line, is formally self-similar but fails to have other fractal characteristics; for instance, it is regular enough to be described in Euclidean terms. Images of fractals can be created using fractal generating software. Images produced by such software are normally referred to as being fractals even if they do not have the above characteristics, as it is possible to zoom into a region of the image that does not exhibit any fractal properties.

DNA also presents significant fractal properties depending on how you define a fractal and depending on the particular genome of the organism in question. It certainly is a compelling way to make sense of seemingly random occurrences in the genome and revealing of a certain level of organization that would otherwise escape recognition. In 1992 Boston researchers looking at the DNA landscape discovered that intron DNA sequences displayed correlations to fractals. Around the same time as self-similarity on the scale of 50 million nucleotides showed up in a study at IBM. Due to base pairing nucleotide sequences can effectively predicted creating a pattern similar to 1/f noise, where f represents the number of bases over which a particular nucleotide repeats, rather than the expected white noise if the pattern were random. As seems to be the case for exon's, Stanley and Golderger found that Prokaryote genomes displayed less correlation, while scaling correlations reached perfect 1/f patterns in invertebrates only to decrease in vertebrates and mammals. [9]



Curriculum Unit 09.05.09 2 of 27

In 1993, this team continued to refine these findings and published three additional, related papers. They knew now, that they were onto something and submitted a paper entitled Fractal Landscapes in Physiology and Medicine: Long-range correlations in DNA sequences and heart rate intervals at the International Symposium in Ascona in May of that same year. Subsequently, in 1995 Stanley and Golderger observed that junk DNA sequences from 40 different species were found to obey Zipf's law and exhibited quite a lot of redundancy as would be expected from a language, which may be required for the regulation of the folding of DNA to fit into the nucleus, after having done a study earlier that year looking at the relationship between Zipf's Law and binary sequences that prompted further investigation into the statistical properties of DNA. [10]

In 1998 the Boston team developed techniques to quantify DNA patchiness and then go on to investigate fractal scaling patterns in heartbeats, neurons and sandstone formation in 1999 [11] as Abramson, Cerdeira & Bruschi explore the Fractal Properties of DNA. [12] In 2000 the Boston team begins to use molecular analysis to identify patterns in protein folding and in 2002 Chinese researchers, at Xiangtan University, introduce a time series model and geometrical point of view to DNA sequence analysis. More recently in a 2007 study Stanley and his team in Boston investigated long-range auto-correlations in both human and rice chromosomes. [13] The Hutchinson metric is a function which measures the discrepancy between two images for use in fractal image processing and can also be applied to describe the similarity between DNA sequences expressed as real or complex genomic signals.

Mathematics makes possible the management and analysis of the massive database of the Human Genome Project or HGP. Numerical analysis, statistics and modeling play a significant role in mapping and sequencing our DNA -- the blueprint for the genetic information that determines what makes each of us unique. Researchers predict that this fusion of mathematics and biology will result in a new era of molecular medicine, when the diagnosis, treatment and prevention of disease will be individual-specific and thus more successful. Inside the nucleus of nearly every cell in our body, a complex set of genetic instructions, (the human genome) is contained on 23 pairs of chromosomes. Chromosomes, long chains made up primarily of DNA (deoxyribonucleic acid), are long, threadlike molecules coiled inside our cells. Each chromosome, in turn, carries genes that look like beads on a string. Genes (short segments of DNA) are packets of instructions for making particular proteins that tell cells how to behave. The hereditary instructions are written in a four-letter code, with each letter corresponding to one of the chemical constituents of DNA (nitrogen-containing chemicals called bases): A (adenine), G (guanine), C (cytosine), T (thymine). The sequence of As, Gs, Cs and Ts constitutes the recipe for a specific protein. Proteins are large, complex molecules made up of amino acids. If the instructions become garbled, the cell can make a wrong protein or make too much or too little of a protein-mistakes that can result in disease.

Scientists estimate that the human genome contains 30,000 to 40,000 genes, and that genes comprise only about 2% of the human genome-the rest consisting of non-coding regions that provide chromosomal structural integrity and regulate where, when, and in what quantity proteins are made. All humans have the same basic set of genes and genomic regulatory regions that control the development and maintenance of biological structures and processes, yet there are differences among us. Therefore the HGP's reference sequence, which is based on samples of a group of individuals, does not represent an exact match of any one person's genome. Another important HGP goal is to identify many of the small DNA regions that vary among individuals and that could underlie disease susceptibility and drug responsiveness.

Mapping is a genetic map that consists of thousands of markers or short, distinctive pieces of DNA, more or less evenly spaced along chromosomes. This map should enable researchers to pinpoint the location of a gene

Curriculum Unit 09.05.09 3 of 27

between any two markers. Physical maps consist of overlapping pieces of DNA spanning an entire chromosome. When the physical maps are complete, investigators can localize a gene to a particular region of a chromosome by using a genetic map, then select and study a specific piece of the physical map, rather than having to search through the entire chromosome all over again.

Sequencing is the ultimate goal of the HGP, to decode, letter by letter, the exact sequence of all 3 billion nucleotide bases that make up the human genome. Computer scientists, biologists, physicists and engineers are all developing automated technologies to reduce the time and cost of sequencing. Once the human genome sequence database is completed for searching the database will lead to understanding this composite of sequences derived from many individuals.

Genome Mathematics:

Numerical analysis DNA is microscopic however; the amount of data it generates is huge. Researchers require advanced numerical techniques to manipulate and make sense of the data.

Statistics has played a part in generating "draft sequence data" mostly 10,000 base-pair fragments whose approximate chromosomal locations are known. Additional sequencing will close gaps and reduce ambiguities. Statistics is also used to design experiments to optimize information extracted from these experiments.

Computational models Researchers attempt to predict molecular behavior by describing DNA and protein molecules with equations that can be solved numerically. The massive amount of data now available allows for more accurate equations on which to base models and the ability to compare predictions with known results.

Topology or the shape and geometry of complex structures are the basic double helix structure of DNA, which provides a information about the molecule, although not complete. The details of the structure and of the different forms of DNA provide information about the biological function of DNA. In addition, the structure and formation of proteins are far more complicated than those of DNA.

Computer graphics make static and mobile images of DNA structures possible, which enables both researchers and laypersons better able to visualize and study the genome.

Microarrays are a relatively new invention that lets scientists measure something they could not measure previously. A microarray measures how much a messenger RNA of a given type is being made in a sample of tissue at a given moment, which gives a good idea of how much of the corresponding protein is being made.

Biological curiosities can be compared and contrasted in mathematics, with results that far exceed chaotic expectations and speculations. DNA is indeed fractal in certain respects of its operation as evidenced by the huge scale and scope of research completed so far. Regardless of the research, because fractals in nature are exceedingly common, their association with DNA should be anticipated. The evolution of diseases and the evolution of medicine are chronologically parallel in that the rise of the former gives rise to the latter, preferably within the same time intervals. Where medicine has failed or failed to be prompt, pandemics, epidemics, and extinction can result. Understanding and managing patterns that arise within this evolutionary dualism can lead to proactive responses to oppose pandemics, epidemics, and extinction, whereas these

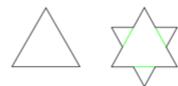
Curriculum Unit 09.05.09 4 of 27

growth patterns and projections are also within the logic and structure of fractals, including the probability to remain constant or mutate.

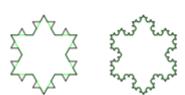
Background

The mathematics behind fractals began to evolve in the 17th century when mathematician and philosopher Leibniz considered recursive self-similarity, although he made the mistake of thinking that only the straight line was a self-similar outcome. It took until 1872 before a function appeared whose graph would today be considered fractal, when Karl Weierstrass gave an example of a function with the non-intuitive property of being everywhere continuous but nowhere differentiable. A class of examples is given by the Cantor sets, Sierpinski triangle and carpet, Menger sponge, dragon curve, space-filling curve, and Koch curve. In 1904, Helge von Koch demonstrated his dissatisfaction with Weierstrass's very abstract and analytic definition by defining a more geometric definition of a similar function, which is now called the Koch curve.

To create a Koch snowflake, one begins with an equilateral triangle and then replaces the middle third of every line segment with a pair of line segments that form an equilateral bump, or three Koch curves. With every iteration, the perimeter of this shape increases by one third of the previous magnitude. The Koch snowflake is the result of an infinite number of these iterations, and has an infinite magnitude, while its area remains finite. The image below illustrates the Koch snowflake and similar constructions that were sometimes called "monster curves."



http://www.kwsi.com/ynhti2009/image02.html



Additional examples of fractals include the Lyapunov fractal and the limit sets of Kleinian groups. Fractals are deterministic, as are all the above, or stochastic and non-deterministic. For example, the trajectories of the Brownian motion in the plane have a Hausdorff dimension of 2.

In 1915, Waclaw Sierpinski constructed his triangle and, one year later, his carpet. Originally these geometric fractals were described as curves rather than the 2D shapes that they are known as in their modern constructions. The animated construction of a Sierpinski Triangle below iterates nine generations of infinite possibilities.

Curriculum Unit 09.05.09 5 of 27



http://www.kwsi.com/ynhti2009/image03.html

In 1918, Bertrand Russell recognized a "supreme beauty" within the emerging mathematics of fractals. The idea of self-similar curves was taken further by Paul Pierre L¨évy, who, in his 1938 paper Plane or Space Curves and Surfaces Consisting of Parts Similar to the Whole described a new fractal curve, the L¨évy C curve. Georg Cantor also gave examples of subsets of the real line with unusual properties--these Cantor sets are also now recognized as fractals. Iterated functions in the complex plane were investigated in the late 19th and early 20th centuries by Henri Poincar¨é, Felix Klein, Pierre Fatou and Gaston Julia. Without the aid of modern computer graphics however, they lacked the means to visualize the beauty of many of the objects that they had discovered.

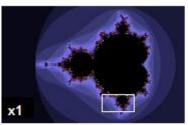
In the 1960s, Beno?t Mandelbrot started investigating self-similarity in papers such as How Long Is the Coast of Britain? Statistical Self-Similarity and Fractional Dimension, which built on earlier work by Lewis Fry Richardson. Finally, in 1975 Mandelbrot coined the word "fractal" to denote an object whose Hausdorff-Besicovitch dimension is greater than its topological dimension. He illustrated this mathematical definition with convincing computer-constructed visualizations. These images captured the popular imagination; many of them were based on recursion, leading to the popular meaning of the term "fractal."

Chaotic dynamical systems are sometimes associated with fractals. Objects in the phase space of a dynamical system can be fractals as in an attractor. Geometrically, an attractor can be a point, a curve, a manifold, or even a complicated set with a fractal structure known as a strange attractor. Objects in the parameter space for a family of systems may be fractal as well. An interesting example is the Mandelbrot set. This set contains whole discs, so it has a Hausdorff dimension equal to its topological dimension of 2, but what is truly surprising is that the boundary of the Mandelbrot set also has a Hausdorff dimension of 2, while the topological dimension is 1, a result proved by Mitsuhiro Shishikura in 1991. Closely related to the Mandelbrot fractal set is the Julia fractal set, as illustrated below.

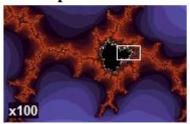
Generating fractals

Techniques for generating fractals, shown at 2000 times magnification of the Mandelbrot set, reveal that the fine detail resembles the full set.

Curriculum Unit 09.05.09 6 of 27



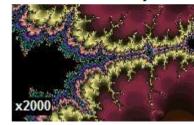
Escape-time fractals



Random fractals



Iterated function systems



Strange attractors

Escape-time fractals are defined by a formula or recurrence relation at each point in a space, such as the complex plane, and are also known as "orbits" fractals. Examples of this type are the Mandelbrot set, Julia set, the Burning Ship fractal, the Nova fractal and the Lyapunov fractal. The 2d vector fields that are generated by one or two iterations of escape time.

- 1. the Mandelbrot set, Julia set, the Burning Ship fractal, the Nova fractal and the Lyapunov fractal. The 2d vector fields that are generated by one or two iterations of escape-time formulae also give rise to a fractal form when points (or pixel data) are passed through this field repeatedly.
- Iterated function systems have a fixed geometric replacement rule. Cantor set, Sierpinski 2. carpet, Sierpinski gasket, Peano curve, Koch snowflake, Harter-Highway dragon curve, T-Square, Menger sponge, are some examples of such fractals.
- Random fractals are generated by stochastic rather than deterministic processes, for example, trajectories of the Brownian motion, L"évy flight, fractal landscapes and the Brownian tree. The latter yields so-called mass- or dendritic fractals, for example, diffusion-limited aggregation or reaction-limited aggregation clusters.
- 4. Strange attractors are generated by iteration of a map or the solution of a system of initial-value differential equations that exhibit chaos.

Classifications

Fractals can also be classified according to their self-similarity, of which there are three types of self-similarity found in fractals:

Exact self-similarity is the strongest type of self-similarity; the fractal appears identical at 1. different scales. Fractals defined by iterated function systems often display exact self-similarity.

Curriculum Unit 09.05.09 7 of 27

Quasi-self-similarity is a lesser form of self-similarity; the fractal appears approximately (but not exactly) identical at different scales. Quasi-self-similar 2. fractals contain small copies of the entire fractal in distorted and degenerate forms. Fractals defined by recurrence relations are usually quasi-selfsimilar but not

exactly self-similar.

Statistical self-similarity is the weakest type of self-similarity; the fractal has numerical or statistical measures which are preserved across scales. Most reasonable definitions of

3. "fractal" trivially imply some form of statistical self-similarity. Fractal dimension itself is a numerical measure which is preserved across scales. Random fractals are examples of fractals which are statistically self-similar, but neither exactly nor quasi-self-similar.

In nature

Approximate fractals are easily found in nature. These objects display self-similar structure over an extended, but finite, scale range. Examples include clouds, snow flakes, crystals, mountain ranges, lightning, river networks, cauliflower or broccoli, and systems of blood vessels and pulmonary vessels. Coastlines may also be considered to approximate fractals in nature.

Trees and ferns are fractal in nature and can be modeled on a computer by using a recursive algorithm. This recursive nature is obvious in these examples: a branch from a tree or a frond from a fern is a miniature replica of the whole: not identical, but similar in nature. The connection between fractals and leaves are currently being used to determine how much carbon is contained in trees. This connection is hoped to help determine and solve the environmental issues of carbon emission and management.

In 1999, certain self similar fractal shapes were shown to have the property of "frequency invariance," which is the same electromagnetic properties no matter what the frequency--from Maxwell's equations (see fractal antenna).

Curriculum Unit 09.05.09 8 of 27

A fractal that models the surface of a mountain (animation)	A fractal fem computed using an iterated function system	Photograph of a romanesco broccoli, showing a naturally occurring fractal	Fractal pentagram drawn with a vector iteration program

In art and architecture

Fractal patterns have been found in the paintings of American artist Jackson Pollock. While Pollock's paintings appear to be composed of chaotic dripping and splattering, computer analysis has found fractal patterns in his work. Decalcomania, a technique used by artists such as Max Ernst, can produce fractal-like patterns. It involves pressing paint between two surfaces and pulling them apart. Fractals are also prevalent in African art and architecture. Circular houses appear in circles of circles, rectangular houses in rectangles of rectangles, and so on. Such scaling patterns can also be found in African textiles, sculpture, and even popular hairstyles.

Applications

As described above, random fractals can be used to describe many highly irregular real-world objects. Other applications of fractals include:

- 1. Classification of histopathology slides in medicine
- 2. Fractal landscape or Coastline complexity
- 3. Enzyme/enzymology and Michaelis-Menten kinetics
- 4. Generation of new music
- 5. Generation of various art forms
- 6. Signal and image compression
- 7. Creation of digital photographic enlargements
- 8. Seismology
- 9. Fractal in soil mechanics

Curriculum Unit 09.05.09 9 of 27

10. Computer and video game design, especially computer graphics for organic

environments and as part of procedural generation

- 11. Fractography and fracture mechanics
- 12. Fractal antennas Small size antennas using fractal shapes
- 13. Small angle scattering theory of fractally rough systems
- 14. T-shirts and other fashion
- 15. Generation of patterns for camouflage, such as MARPAT
- 16. Digital sundial
- 17. Technical analysis of price series, as in the Elliott fractal principle

Consequently, this curriculum unit should increase preparation for assigned courses in the curricular areas of Math and Physics by exploring the predictors and mathematical probabilities of Evolutionary Medicine, and by discovering graph-associated and data-driven patterns and fractals of evolution that had been ignored by medicine, which focused instead upon proximate mechanical causes similar to the hard sciences. Promoted by a plethora of voices representing the medical industry, medicine has modeled itself after a mechanical physics, derived from Galileo, Newton, and Descartes. This model clearly mitigates medicine as mechanistic, materialistic, reductionistic, linear-causal, and deterministic or capable of precise conceptual predictions.

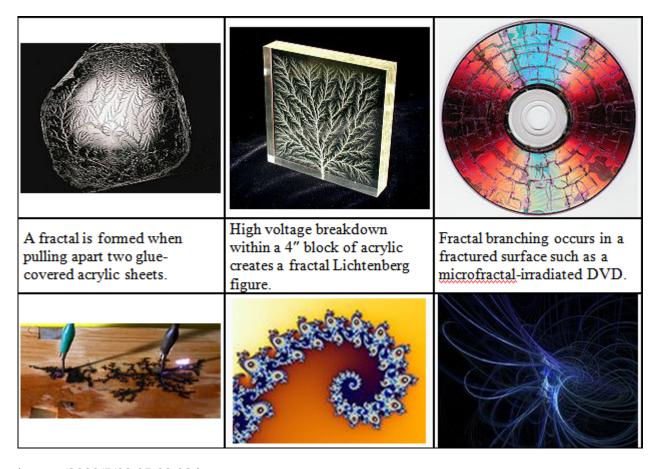
In numerical analysis, statistics, computational models, differential equations, and dynamical systems:

Topology deals with the shape and geometry of complex structures. The basic double helical structure of DNA provides a good deal of information about the molecule, but it is not

- 1. complete. The details of the structure and of the different forms of DNA provide information about the biological function of DNA. In addition, the structure and formation of proteins are far more complicated than those of DNA.
- 2. Computer graphics make static and mobile images of DNA structures possible, which enables both researchers and laypersons better able to visualize and study the genome. [14]

Concurrently, the search reaches for understanding diseases, while explaining the symptoms, signs, and causes that manifest in single, materialistic, anatomical or structural changes within the body, such as in genes and their products, ostensibly necessary process directly or linearly, by infectious, toxic, or traumatic agents. In addition to the known results for picking geometric objects from points in or on the boundary of other geometric objects, this seminar will contribute to preparations for: Bertrand's Problem, Buffon-Laplace Needle Problem, Buffon's Needle Problem, Circle Inscribing, Computational Geometry, Integral Geometry, Point Picking, Stochastic Geometry, and Sylvester's Four-Point Problem.

Curriculum Unit 09.05.09 10 of 27



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Fractals of bacteria colonies adopt the fractal formed appearances of trees and ferns. In the late 1980s, Fujikawa and Matsushita studied colonies of the bacteria Bacillus subtilis 168 (B 168), common in soil, under stressed conditions causing the colonies to adopt a fractal form. Experimental parameters include: the hardness of the agar on which the bacteria grow and the nutrient concentration. Friendly conditions, soft agar and abundant nutrients, result in compact growth with smooth boundaries. In more unfriendly conditions, the bacteria can grow in patterns on the left, resembling DLA clusters on the right. Diffusion-Limited Aggregation, or DLA, is an extraordinarily simple computer simulation of the formation of clusters by particles diffusing through a medium that jostles the particles as they move. Evolution in organisms and in fractals expands in the outward direction with self-representation. This accounts for both individual organisms as well as the populations they comprise. When geometric progressions regress and fractals collapse, shrinking populations are represented.

Important researchers in evolutionary medicine include: Randolph M. Nesse, George C. Williams, Paul W. Ewald, James McKenna, and Rainer H. Straub. George C. Williams was the first to apply evolutionary theory to health in the context of senescence. Also in the 1950s, John Bowlby approached the problem of disturbed child development from an evolutionary perspective upon attachment. An important theoretical development was Nikolaas Tinbergen's distinction made originally in ethology between evolutionary and proximate mechanisms.

Adaptations include:

Curriculum Unit 09.05.09 11 of 27

 $^{1. \}label{eq:continuous}$ The evolution of pathogens in terms of their virulence, resistance to antibiotics, and subversion of an individual's immune system.

- 2. The processes, constraints and trade-offs of human evolution.

 The evolved responses that enable individuals to protect, heal, and recuperate themselves
- 3. from infections and injuries such as immunity, fever, and sickness behavior, and the processes that regulate their deployment to maximize fitness.
 - How past adaptation of early humans to their ancestral environment now affects
- 4. contemporary humans with their different diet, life expectancy, degree of physical exercise, and hygiene.

Key developments include the paper of Paul Ewald in 1980, "Evolutionary Biology and the Treatment of Signs and Symptoms of Infectious Disease," and that of Williams and Nesse in 1991, "The Dawn of Darwinian Medicine." The latter papers evolved into a book, Why We Get Sick, published as Evolution and healing in the United Kingdom. In 2008, an online journal started: Evolution and Medicine Review. While the two main mechanisms that produce evolution are natural selection and genetic drift, natural selection favors genes that improve the capacity for survival and reproduction, whereas genetic drift is random change in the frequency of alleles, caused by the random sampling of a generation's genes during reproduction. The significance of natural selection and genetic drift in populations vary depending upon the strength of the selection and the effective population size, which is the number of individuals capable of reproducing. [1]

Natural selection usually predominates in large populations however; genetic drift dominates in small populations. The dominance of genetic drift in small populations encourages deleterious effects or mutations. Alternatively, population bottlenecks, where the population shrinks temporarily and therefore loses genetic variation, result in a more uniform population. Consequently, changing population size can dramatically influence the course of evolution. In the 1930s, Darwinian natural selection was combined with Mendelian inheritance to form the modern evolutionary synthesis, which connected the units of evolution, or genes and the mechanism of evolution, or natural selection. This powerful explanatory and predictive theory directs research by constantly raising new questions, and it has become the central organizing principle of modern biology, providing a unifying explanation for the diversity of life on Earth.

Essential Questions

- 1. Are these patterns the result of simple physical processes, or do they represent selforganization and coordination on multiple levels?
- 2. Certainly, different causes can produce the same effect: does the existence of fractal bacteria colonies favor proximate or evolutionary mechanism over the other?
- 3. Why have 3 billion years of evolution given Nature ample opportunity to exclusively discover and exploit purely physical processes?
- 4. Would exploring algorithms that generate predictable fractals define patterns that would result from proximate and evolutionary mechanisms?

http://www.kwsi.com/ynhti2009/image05.html

Curriculum Unit 09.05.09 12 of 27

Algorithms:

- 1. Escape time algorithm
 - a) Boolean version (draws M-set and its exterior using 2 colors) -- Mandelbrot algorithm
 - b) discrete (integer) version -- level set method (LSM/M); draws Mandelbrot set and color bands in its exterior
 - c) continuous version
 - d) level curves version -- draws lemniscates of Mandelbrot set -- boundaries of Level Sets
 - e) decomposition of exterior of Mandelbrot set

- 2. Complex potential
 - a) Hubbard-Douady (real) potential of Mandelbrot set (CPM/M) radial part of complex potential
 - b) external angle of Mandelbrot set -- angular part of complex potential
 - c) abstract M-set
- 3. Distance estimation method for Mandelbrot set
 - a)exterior distance estimation -- Milnor algorithm (DEM/M)
 - b) interior distance estimation
- 4. Algorithm used to explore interior of Mandelbrot set
 - a) period of hyperbolic components
 - b) multiplier of periodic orbit (internal rays(angle) and internal radius)
 - c) bof61 and bof60

Every algorithm can be implemented in sequential or parallel version. Mirror symmetry can be used to speed-up calculations.

Escape time algorithm

The simplest algorithm for generating a representation of the Mandelbrot set is known as the escape time algorithm. A repeating calculation is performed for each x, y point in the plot area and based on the behavior of that calculation, a color is chosen for that pixel.

The x and y locations of each point are used as starting values in a repeating, or iterating process of calculations. The result of the previous iteration defines the starting values for the next iteration. The result of the previous iteration is also checked during the next iteration to see if a critical escape condition or bailout has been reached. If and when that condition is reached, the calculation is stopped, the pixel is drawn, and

Curriculum Unit 09.05.09 13 of 27

the next x, y point is examined. For some starting values, escape occurs quickly, after only a small number of iterations. For starting values very close to but not in the set, it may take hundreds or thousands of iterations to escape. For values within the Mandelbrot set, escape will never occur. The higher the maximum number of iterations, the more detail and subtlety emerge in the final image, but the longer time it will take to calculate the fractal image.

Escape conditions can be simple or complex. Because no complex number with a real or imaginary part greater than 2 can be part of the set, a common bailout is to escape when either coefficient exceeds 2. A more computationally complex method, but which detects escapes sooner, is to compute the distance from the origin using the Pythagorean Theorem, and if this distance exceeds two, the point has reached escape. More computationally-intensive rendering variations such as Buddhabrot detect an escape, then use values iterated along the way.

The color of each point represents how quickly the values reached the escape point. Often black is used to show values that fail to escape before the iteration limit, and gradually brighter colors are used for points that escape. This generates a visual representation of how many cycles were required before reaching the escape condition.

For programmers

The definition of the Mandelbrot set, together with its basic properties, suggests a simple algorithm for drawing a picture of the Mandelbrot set. The region of the complex plane under consideration is subdivided into a certain number of pixels. To color any such pixel, let c be the midpoint of that pixel. The critical value c under P_c , is iterated checking at each step whether the orbit point has a modulus larger than 2.

If this is the case, we know that the midpoint does not belong to the Mandelbrot set, and the pixel is colored. Either it is colored white to get the simple mathematical image or it is colored according to the number of iterations used to get the well-known colorful images. Otherwise, iterating is continued for a certain number of steps that is large but fixed, after which this parameter can probably be placed in the Mandelbrot set, or at least very close to it, and color the pixel black.

In pseudocode, this algorithm would look as follows:

For each pixel on the screen do:

```
iteration = 0
max iteration = 1000
while (x*x + y*y = (2*2) AND iteration max_iteration)
{
xtemp = x*x - y*y + x0
y = 2*x*y + y0
x = xtemp
iteration = iteration + 1
}
if ( iteration == max_iteration )
then
color = black
else
color = iteration
plot(x0,y0,color)
}
http://www.kwsi.com/ynhti2009/image06.html
```

Lesson Plans

- 1. Lesson One -collect data, observations and draw conclusions (defined below).
- 2. Lesson Two generate fractals, observations and draw conclusions (defined below)...
- 3. Lesson Three extrapolate geometric progressions, observations and draw conclusions (defined below)..
- 4. Lesson Four mutations, observations and draw conclusions (student defined).

Curriculum Unit 09.05.09 15 of 27

Lesson Number 1 - Functions as Mathematical Models of Proximate and Evolutionary Medicine Phenomena

Objective(s) - students will be able

- 1. To discuss and provide examples of how mathematics is used to describe nature, and Proximate and Evolutionary Medicine Phenomena in particular
- 2. To define and provide an example of a function and a mathematical model
- 3. To provide examples of dimensions and the units used to measure them
- 4. To apply the concepts of function, independent and dependent variable to describe relationships between natural phenomena using multiple representations of functions.
- 5. To classify the relationship between pairs of variables associated with Proximate and Evolutionary Medicine Phenomena as linear, quadratic, or exponential
- 6. To pose questions about Proximate and Evolutionary Medicine Phenomena that may be answered by using a mathematical model
- 7. Describe the difference between Proximate and Evolutionary Medicine Phenomena
- 8. Define proximate and evolutionary medicine, and fractal

Prerequisite skills

graphing two-variable data, evaluating expressions, translating verbal phrases and sentences to algebraic expressions and equations, solving equations, creating and interpreting tables and graphs on coordinate plane

Materials

Ruler or tape measure, thermometer, clock, scale

Worksheet or text with tables of different types of function, without the equations

Relevant Vocabulary, Terms and Symbols

domain, independent variable, dependent variable, f(x) = y, dimension, fractal, function, mapping diagram, proximate and evolutionary medicine, range, unit, vertical line test

Strategy

Students should be prompted to discuss different types of phenomena that are measured. They should also discuss what types of instruments are used for the measurements. This discussion should result in defining dimensions. As a class, we list different units that are used to measure the dimensions of mass, transfer, magnitude, time and temperature. Review the definition of function. Use the student as function input metaphor - can't go to two places at once. Encourage students to come up with measureable quantities and measurement units. Prepare a measurement activity that involves a simple linear function. Prepare tables of different types of functions related to Proximate and Evolutionary Medicine Phenomena for review of function types. Prompt students to classify each table as a type of function. Describe natural pandemics and epidemics, the different types of Proximate and Evolutionary Medicine Phenomena, and their characteristics. Use the case studies to provide an example of each type of disaster to be studied. An overhead slide show

Curriculum Unit 09.05.09 16 of 27

would nicely show the results of the disasters. Ask questions about the characteristics of Proximate and Evolutionary Medicine Phenomena, i.e. "are these two related? How is that so?" Provide encouragement and feedback

Student tasks

Form small groups

List examples of quantities that we measure in the environment

Classify each type of quantity by its dimension, and give an example of units

Discuss how some pairs of quantities may be related

Find two quantities that have a functional relationship

Describe the functional relationship in words using "is a function of" and in symbols using a = f(b)

Present one of your functions to the class, with both verbal and symbolic representations

Engage in measurement activity involving magnitude, time, and force, using ruler, clock, and scale Any distance, rate, and time problem would suffice.

Classify a function represented with a table as linear, quadratic or exponential.

Answer elementary questions about the Proximate and Evolutionary Medicine Phenomena discussed, define terms.

Questions

For each of the following pairs of phenomena, determine the dimension and possible units of each variable, and determine if there may be a functional relationship between the two. Then identify the independent and dependent variables, and write a sentence that describes the relationship.

Time of day & temperature

Month & temperature

Location & weather

Number of deaths & proximate and evolutionary medicine magnitude

Give examples of dimensions and units

What is the difference between an epidemic and a pandemic?

Curriculum Unit 09.05.09 17 of 27

What questions can be asked about these events?

What type of mathematics would create answers to these questions?

Lesson Number 2 - Modeling Proximate and Evolutionary Medicine Height with Quadratic and Root Functions

Objective(s) - students will be able

- 1. To use mathematical models to describe observed relationships between characteristics of Proximate and Evolutionary Medicine Phenomena when values of some variables are known
- 2. To derive mathematical models from existing equations and relations (solve multivariate equations for one of the variables)
- 3. To provide examples of the application of a quadratic or square root function to Proximate and Evolutionary Medicine Phenomena
- 4. To represent functions as equations, tables, graphs, and verbal descriptions
- 5. To describe the domain and range of functions used to model Proximate and Evolutionary Medicine Phenomena
- 6. To draw and label a simple pictorial representation of a fractal
- 7. To calculate fractal magnitudes, periods, depths, and frequencies of fractals
- 8. To describe the relationship between fractal magnitude and fractal frequency in at least two different ways

Prerequisite skills

Vertex form of quadratic function, translations of parabolas, solving equations using square roots

Materials

Provide Graphing calculator, graph paper, worksheets with student tasks, questions, and a place to write answers.

Relevant Vocabulary, Terms and Symbols

Define axis of symmetry, fractal, maximum, minimum, parabola, vertex, and x-intercept.

Strategy

A fractal can be modeled by having two students hold a piece of rope in front of the class. One student propagates a fractal, and the other students can be prompted to estimate the height of the fractal. Another student propagates a larger fractal, and again the students can estimate the height of the second fractal. A discussion explaining the definition of amplitude follows. The amplitude here can be related to water depth instead of fractal height. Provide one form each of the equations for proximate and evolutionary medicine and fractal. Prompt students to derive the other form of the relation. Provide students with specific calculation questions that can be solved using the presented equations. Provide encouragement and feedback

Student tasks

Curriculum Unit 09.05.09 18 of 27

Describe a fractal, its characteristics, and its properties.

Give examples of fractals.

Give examples of fractals representing proximate and evolutionary medicine.

Take notes on proximate and evolutionary medicine equations.

Attempt to solve equations for the independent variables.

Answer questions that arise from the anatomy of fractals.

Questions

Define a fractal, proximate and evolutionary medicine.

Find the magnitude of a fractal associated with proximate and evolutionary medicine.

Find the period or frequency of a fractal associated with proximate and evolutionary medicine with given frequency and fractal magnitude

Find the frequency of a proximate and evolutionary medicine with given fractal magnitude and period

Find the height of a proximate and evolutionary medicine with given frequency

Find the frequency of a proximate and evolutionary medicine with given water depth

Find the energy of a proximate and evolutionary medicine with given water depth and fractal magnitude

Find the fractal magnitude of a proximate and evolutionary medicine with given water depth and energy

Find the height of a proximate and evolutionary medicine with given fractal magnitude and energy

What is a shallow water fractal?

What are some of the difference between fractals?

What scale is used to measure magnitude?

Find the magnitude of a fractal with given wind speed

Find the wind speed of a fractal with a given magnitude

Compare two fractals with two given sets fractal magnitude and height

What is the relationship between these magnitudes compared to their heights?

Which natural phenomena have quadratic relationships?

Write a sentence describing the relationship between proximate and evolutionary medicine height, fractal magnitude and frequency

Write a sentence describing the relationship between fractal frequency and magnitude

Curriculum Unit 09.05.09 19 of 27

Lesson Number 3 - Modeling Proximate and Evolutionary Medicine Magnitude and Population Growth using Exponential and Logarithmic Functions

Objective(s) - students will be able

- 1. To physically model a proximate and evolutionary medicine and describe how friction and surface area relate to proximate and evolutionary medicine magnitude
- 2. To describe the relationship between proximate and evolutionary medicine magnitude and energy in at least two different ways
- 3. To define moment, magnitude, and moment magnitude
- 4. To describe the relationship between moment and moment magnitude in at least two different ways
- 5. To describe the relationship between proximate and evolutionary medicine magnitude and frequency of occurrence in at least two different ways
- 6. To apply exponential and logarithmic functions to the relationship between proximate and evolutionary medicine magnitude and energy released
- 7. To apply exponential and logarithmic functions to the relationship between time and population size

Prerequisite skills

Order of operations, rules of exponents, graphing functions manually and with graphing calculator, solving equations by taking logarithms and exponentiating

Materials

Sponges of different sizes, all with a flat sides, water

Graphing calculator, graph paper, worksheets including discussion prompts and calculation exercises

Relevant Vocabulary, Terms and Symbols

Exponential Equations, Exponents, Logarithmic Equations, and Logarithms

Strategy

The cause of a proximate and evolutionary medicine can be simply modeled using a sponge, and a piece of string. If only one sponge is available, this exercise can be done as a classroom demonstration of transference. Otherwise, students may be divided into groups, each of which has one type of sponge, and a piece of string. Each group places a saturated sponge on a table a given distance from another sponge. Students then incrementally exert pressure on the saturated sponges, which are on the table. As a class, we estimate the surface areas of the sponges that are in contact with each other on the table. As a class we discuss and record how much pressure it takes for each sponge to transfer water to the neighboring sponge. The pressure resembles the amount of transference required to yield proximate and evolutionary alterations. The area of the sponge represents the area of transfer during a proximate and evolutionary medicine. Students should conclude that the larger sponge yields larger proximate evolution. Students should be prompted to generalize that the larger the area of the sponge, the larger the potential for proximate and

Curriculum Unit 09.05.09 20 of 27

evolutionary medicine. This discussion segues into the discussion of proximate and evolutionary medicine magnitude. The effects of a proximate and evolutionary medicine on a population may be shown by adjusting the distances between the sponges on the table. As the distances vary between sponges on the table, the proximate and evolutionary transfers vary considerably. Begin discussion of population by asking students what the local, state, national, and global populations are. These would be good questions for students to research independently. Present graphical representations of population fluctuations and growth. Provide notes on proximate and evolutionary medicines and population growth. Provide one version of each equation that will be used in the exercises. Encourage and provide feedback.

Student tasks

Participate in sponge and water exercise
Record data
Participate in concluding discussion
Take notes on proximate and evolutionary medicines and population growth,
 particularly equations
Attempt to solve each equation for the independent variable
Practice calculations on worksheet
Respond to and discuss open-ended questions

Questions

Define proximate and evolutionary medicine

Name two scales used to measure proximate and evolutionary medicine magnitude
Find the event of a proximate and evolutionary medicine with a given magnitude
Find the event magnitude of proximate and evolutionary medicine with a given
Find the magnitude of proximate and evolutionary medicine that released a given amount of lifealtering characteristics

Find the amount of life-altering characteristics released in proximate and evolutionary medicine
Find the recurrence interval of proximate and evolutionary medicine with a given
minimum

What is the current population of the United States?

What is the current population of the earth?

How can the growth rate of a population be found using the birth rate and death rate?

At the current growth rate, in what year will the world population be 10 billion?

Curriculum Unit 09.05.09 21 of 27

At the current growth rate, what will the world population be in 2050? What effects does the human population have on other species of animals and plant? And, if any, are the effects on natural resources? Which natural phenomena have exponential relationships?

Website(S)

http://www.kwsi.com/ynhti2009/

http://www.kwsi.com/ynhti2009/image02.html

http://www.kwsi.com/ynhti2009/image03.html

http://www.kwsi.com/ynhti2009/image04.html

http://www.kwsi.com/ynhti2009/image05.html

http://www.kwsi.com/ynhti2009/image06.html

Curriculum Unit 09.05.09 22 of 27

Glossary of Terms

Apollonian gasket: or Apollonian net is a fractal generated from triples of circles, where any circle is tangent to two others, named after Greek mathematician Apollonius of Perga.

Bacteriophages: any one of a number of viruses that infect bacteria, from "bacteria" and the Greek Φ?ΓΕΙΝ phagein "to eat."

Bifurcation theory: is the mathematical study of changes in the qualitative or topological structure of a given family. Examples of such families are the integral curves of a family of vector fields or, the solutions of a family of differential equations.

Butterfly effect: is a phrase that encapsulates the more technical notion of sensitive dependence on initial conditions in chaos theory. Small variations of the initial condition of a dynamical system may produce large variations in the long term behavior of the system.

Chaos theory: a branch of mathematical and physical theory that deals with the nature and consequences of chaos and chaotic systems.

Complexity: a whole made up of complicated or interrelated parts.

Constructal theory: is the mental viewing that the generation of design, configuration, pattern, and geometry in nature is the physics phenomenon that unites all animate and inanimate systems, and that this phenomenon is covered by the Constructal Law stated by Adrian Bejan in 1996.

Contraction mapping theorem: or contraction mapping principle is an important tool in the theory of metric spaces; it guarantees the existence and uniqueness of fixed points of certain self maps of metric spaces, and provides a constructive method to find those fixed points. The theorem is named after Stefan Banach (1892-1945), and was first stated by him in 1922.

Diamond-square algorithm: is a method for generating highly realistic heightmaps for computer graphics. It is a slightly better algorithm than the three-dimensional implementation of the midpoint displacement algorithm which produces two-dimensional landscapes, and is also known as the random midpoint displacement fractal, the cloud fractal or the plasma fractal, because of the plasma effect produced when applied.

DNA knots: contains the genetic information that allows all modern living things to function, grow and reproduce however, it is unclear how long in the 4-billion-year history of life DNA has performed this function, as it has been proposed that the earliest forms of life may have used RNA as their genetic material.

Droste effect: The Droste effect is a Dutch term for a specific kind of recursive picture, one that in heraldry is termed mise en abyme. An image exhibiting the Droste effect depicts a smaller version of itself in a place where a similar picture would realistically be expected to appear. This smaller version then depicts an even smaller version of itself in the same place, and so on. Only in theory could this go on forever; practically, it continues only as long as the resolution of the picture allows, which is relatively short, since each iteration exponentially reduces the picture's size. It is a visual example of a strange loop, a self-referential system.

Evolution: is the change in the genetic material of a population of organisms from one generation to the next. Small differences can accumulate over time with each generation, which can manifest substantial changes in the organisms, and the emergence of new species.

Feigenbaum function: has been used to describe two different functions introduced by the physicist Mitchell Feigenbaum, in the study of dynamical systems.

Curriculum Unit 09.05.09 23 of 27

Fractal art: is created by calculating fractal objects and representing the calculation results as still images, animations, music, or other media.

Fractal compression: applies algorithms convert geometric shapes into mathematical data called fractal codes which are used to recreate the encoded image. Fractal compression differs from pixel-based compression schemes such as JPEG, GIF and MPEG since no pixels are saved. Once an image has been converted into fractal code its relationship to any specific resolution is irrelevant, and it becomes resolution independent.

Fractal flames: are a member of the iterated function system class of fractals created by Scott Draves in 1992, and differ from ordinary iterated function systems in three ways: nonlinear functions are iterated instead of affine transforms; log-density display instead of linear or binary, a form of tone mapping; and color by structure or by the recursive path taken, instead of monochrome or by density.

Fractals: any of various extremely irregular curves or shapes for which any suitably chosen part is similar in shape to a given larger or smaller part when magnified or reduced to the same size

Fractal landscape: is a surface generated using a stochastic algorithm designed to produce fractal attributes that mimic the appearance of natural terrains; the result of which is not a deterministic fractal surface, but rather a random surface which displays fractal attributes

Fractal transform: is a technique invented by Michael Barnsley et al. to perform lossy image compression. This first practical fractal compression system for digital images resembles a vector system using the image itself as the codebook.

Fractint: is a freeware software package that can render and display many kinds of fractals. Its name comes from the words fractal and integer, since the first versions of it computed fractals by using only integer arithmetic (also known as fixed-point arithmetic), which led to much faster rendering on x86 computers without math coprocessors.

Fracton: is a collective quantized vibration on a substrate with a fractal structure, and are the fractal analog of phonons.

Geometric progressions: a sequence, such as 1, $\frac{1}{2}$, $\frac{1}{4}$, in which the ratio of a term to its predecessor is always the same, also called a geometrical progression or geometric sequence.

Graftal: or L-system is a formal grammar used in computer graphics to recursively define branching tree and plant shapes in a compact format.

Greeble: or nurnie is a small piece of detailing added to break up the surface of an object to add visual interest to a surface or object, particularly in movie special effects.

Iteration: a procedure in which repetition of a sequence of operations yields results successively closer to a desired result.

Lacunarity: is a measure of how a fractal fills space, and is used to further classify fractals and textures which, while sharing the same fractal dimension, appear very different visually. Dense fractals have a low lacunarity, and as the coarseness of the fractal increases, so does the lacunarity.

List of fractals by Hausdorff dimension: one of the essential features of a fractal is that its Hausdorff dimension strictly exceeds its topological dimension.

Mathematical knots: is an embedding of a circle in 3-dimensional Euclidean space.

Curriculum Unit 09.05.09 24 of 27

Mitochondria: any of various round or long cellular organelles of most eukaryotes that are found outside the nucleus, produce energy for the cell through cellular respiration, and are rich in fats, proteins, and enzymes.

Newton fractal: is a boundary set in the complex plane which is characterized by Newton's method applied to a fixed polynomial.

Recursion: the determination of a succession of elements, such as numbers or functions, by operation on one or more preceding elements according to algorithms, rules, or formulas, involving a finite number of steps or iterations.

Sacred geometry: Sacred geometry is geometry used in the design of sacred architecture and sacred art, with the basic belief is that geometry and mathematical ratios, harmonics and proportion are also found in music, light, and cosmology.

Self-reference: referring to, or towards oneself or itself.

Sierpinski triangle: a fractal named after the Polish mathematician Wac?aw Sierpi"½ski who described it in 1915, also called the Sierpinski gasket or the Sierpinski Sieve.

Space-filling curve: a continuous curve in 2, or 3, or higher dimensions can be thought of as the path of a continuously moving point, and to eliminate the inherent vagueness of this notion, brought to light by Peano's discovery, Jordan in 1887 introduced the following rigorous definition, which has since been adopted as the precise description of the notion of a continuous curve.

Strange loop: A strange loop is a hierarchy of levels, each of which is linked to at least one other by some type of relationship.

Tripanosomes: any of a genus (Trypanosoma) of parasitic flagellate protozoans that infest the blood of various vertebrates including humans, are usually transmitted by the bite of an insect, and include some that cause serious diseases, such as sleeping sickness and Chagas' disease.

Turbulence: irregular motion or agitation especially when characterized by up-and-down currents

Student Resources:

- [1] http://www.math.com/students/wonders.html
- [2] http://mathforum.org/library/topics/fractals/
- [3] http://www.cln.org/themes/fractals.html

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- [1] Nesse, Randolph M. and Williams, George C. Why We Get Sick: the New Science of Darwinian Medicine. New York, Vintage Books, a division of Random House, Inc., 1995.
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Curriculum Unit 09.05.09 25 of 27

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- [7] Barnsley , Michael Fielding, Fractals Everywhere: The First Course in Deterministic Fractal Geometry (Hardcover), Cambridge University Press, 1988.
- [8] Bates, Andrew D. and Maxwell, Anthony, DNA Topology, Oxford University Press, 2005.
- [9] http://polymer.bu.edu/hes/articles/pbghs Long range correlations in Nucleotide sequences
- [10] http://polymer.bu.edu/hes/articles/mbghp Systematic analysis of coding and non-coding DNA sequences using methods of statistical linguistics
- [11] http://polymer.bu.edu/hes/articles/hbbgi Scaling in nature from DNA to heartbeats to weather
- [12] http://www.iop.org/EJ/abstract/1009-1963
- [13] http://polymer.bu.edu/hes/articles/psdzs
- [14] http://www.mathaware.org/mam/02/essay1.html
- [15] http://www.mathaware.org/mamdynamic/activities/
- [16] http://polymer.bu.edu/hes/articles/pbghs

Appendix:

Alignment with the NCTM standards requires that the mathematics curriculum should make mathematics more accessible and relevant to students. These developed concepts and skills should be integrated throughout all subject areas.

The following standards are addressed within this curriculum unit:

Standard 8: Communication.

The communication standard states that students should be given the opportunity to:

- 1. Organize and consolidate their understanding of mathematics through communication.
- 2. Communicate their mathematical thinking coherently and clearly.
- 3. Analyze and evaluate their mathematical thinking and strategies to others.
- 4. Use the language of mathematics to express mathematical ideas.

Standard 9: Connections.

This standard states that:

	Students should be given the opportunity to recognize and use connections among mathematical ideas. Recognize and use mathematics in contexts outside mathematics.
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Curriculum Unit 09.05.09 27 of 27