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ents about ionic mechanisms? Are ıeed the calcium besides the sodium lifferential equations and, say, more

ve tried to look at phase resetting Clay, Shrier, and others. The ionic nable agreement with most of the odel, you need at least two variables ıe ionic models try to use the most the computer experiments on the s.

ry to observe a kind of competition heart?

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ınt sorts of bistability can arise in / delicate operation to observe it in ied to do it), but it does exist.

rain rhythms, but it is very difficult m. If we start to learn something

/ould say that the heart is simpler

Fractal Modeling of Biological Structures

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INTRODUCTION

The purpose of this paper is to introduce to a general audience of scientists some recent mathematical results and to show how they can be applied to the construction of geometrical models for physical structures. Euclidean geometry works well to describe the conformation of elements in a building. However, it is an inefficient tool for modeling the placement of a quarter of a million pine needles on a pine tree. The basic tools of Euclidean geometry are readily available; they are straightedge and compass, and include some knowledge of how to write down equations for lines and circles in the Cartesian plane. Here, in equally simple terms, we present a basic tool for working with fractal geometry.

Possible applications of the technique include the construction of geometrical models for features of plants; the spread of a virus on the surface of a human lung; the blood system; tissue masses; dynamical processes, such as growth of plants or networks; and functions on biological structures, such as temperatures on ferns.

Some precisions are in order: (1) By a fractal, we mean here any subset of R^n (typically $n = 2$, 3, and 4) that possesses features that are not simplified by magnification (observation at successively higher visual resolution). In two dimensions, a location on a set is simplified by magnification if it reveals a straight-line segment or isolated point in the asymptotic limit of infinite magnification. This definition is more general than the usual one that states that the Hausdorff-Besicovitch dimension of the set exceeds its topological dimension. (2) A set, such as a Sierpinski Triangle or Classical Cantor Set, which is made exactly of "little copies of itself," is likely to be a fractal; however, in the sense and spirit with which we use the word, it would be a very special case. The fractal geometrical models that we describe here are, in general, much more complicated. Features that are apparent at one location may not be present at other locations nor be retrieved upon closer inspection. (3) We are concerned with deterministic geometry. Thus, any model produced will always be the same subset of R^n irrespective of how many times it is regenerated. We are not concerned with random fractal geometries. Interest in the latter resides in their statistical properties; deterministic fractals may be used to model the exact structure of a specific object over a range of scales. (4) All geometrical models for physical entities are inevitably wrong at some high enough magnification. The architect's drawing of a straight line representing the edge of a roof breaks down as a model if it is examined closely enough. On fine enough scales, the edge of the roof is wriggly, while the (intended) drawing remains endlessly flat. Fractal geometry can provide a better model for the edge of the roof: the model may appear as straight at one scale of observation and to have the right kind of wriggliness at another; however, in the end, it too will be wrong because of the dual nature of matter.

ITERATED FUNCTION SYSTEMS: A WORKSHOP FOR FRACTAL GEOMETRY

The terminology, Iterated Function System (IFS), was introduced by Barnsley and Demko[1] to describe a convenient framework for understanding fractal geometry. This name includes reference to the fact that an IFS has much in common with a dynamical system. Basic work relating to this framework has been described by Hutchinson,[2] Moran,[3] Diaconis and Shashahani,[4] and Dubins and Freedman.[5] Mandelbrot[6] uses the framework implicitly in special cases. Most results referred to here are instances of more general recent theorems due to Demko, Elton, Geronimo, and others.[7-9]

Let K denote one of the spaces R^n ($n = 2$, 3, or 4). Let $W{:}K \rightarrow K$ be a continuous mapping. For example, with $n = 2$, we will usually be concerned with mappings of the special form:

$$W\begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} a & b \\ c & d \end{pmatrix}\begin{pmatrix} x \\ y \end{pmatrix} + \begin{pmatrix} e \\ f \end{pmatrix}.$$

The symbols a, b, c, d, e, and f are real constants that specify the transformation. Here, (x, y) are the coordinates of a point before the transformation has been applied and $(ax + by + e, cx + dy + f)$ are the coordinates afterwards. Such a transformation is said to be affine because it takes straight lines to straight lines. For example, W will typically map a square to a parallelogram, as illustrated in FIGURE 1.

A continuous mapping $W{:}K \rightarrow K$ is said to be contractive if it always decreases the distance between points. Let the distance between two points P and Q in K be denoted $|P - Q|$. Then W is contractive with contractivity factor S (such that $0 \leq S < 1$) if

$$|W(P) - W(Q)| \leq S\,|P - Q|$$

for all pairs of points P and Q in K. For example, the affine map described above will be contractive if the numbers a, b, c, and d are sufficiently small. A suitable choice would be $a = 0.7$, $b = 0.1$, $c = -0.3$, and $d = 0.5$.

The space K, together with a finite set of continuous contractive mappings $W{:}K \rightarrow K$, say $W_1, W_2, \ldots, W_N$, provides an example of an Iterated Function System (IFS). Here is an example of an IFS with $N = 2$:

$$W_1\begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} 0.2 & 0.3 \\ -0.1 & 0.5 \end{pmatrix}\begin{pmatrix} x \\ y \end{pmatrix} + \begin{pmatrix} -0.1 \\ 18 \end{pmatrix};$$

$$W_2\begin{pmatrix} x \\ y \end{pmatrix} = \begin{pmatrix} 0.1 & 0.5 \\ 0.7 & 0.1 \end{pmatrix}\begin{pmatrix} x \\ y \end{pmatrix} + \begin{pmatrix} -1.4 \\ 109 \end{pmatrix}.$$

We will always associate a probability P_n with a map W_n such that $P_1 + P_2 + \ldots + P_N = 1$. In the last example, we might choose $P_1 = 0.39$ and $P_2 = 0.51$.

The fundamental tool of fractal
for fractal sets is the following beaut

THEOR

Let $\{K, W_1, W_2, \ldots, W_N\}$ be an
contractivity factor S (such that 0
closed bounded) set A in K so that

A

Here, we use the notation of $W_n($
the same as the union of the images

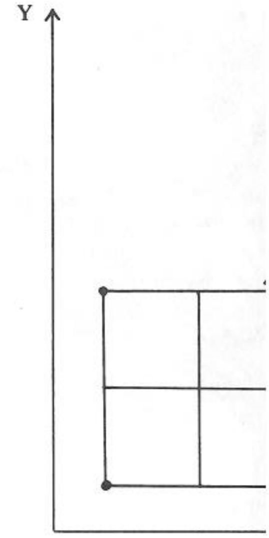


FIGURE 1. An affine transformati

if it is contained in an n-dimension
contains all its boundary points.) W
An example of an attractor of a
affine maps and is specified by thi
features: (1) The image as a whole
uniformly shrunken copies of itself.
reveal exact copies of the original.
under affine deformation. For insta
in the image, along with skewed sm

The fundamental tool of fractal geometry that allows one to write down formulas for fractal sets is the following beautiful result.

THEOREM ON EXISTENCE

Let $\{K, W_1, W_2, \ldots, W_N\}$ be an IFS where each mapping W is contractive with contractivity factor S (such that $0 < S < 1$). Then, there is exactly one (nonempty closed bounded) set A in K so that

$$A = \bigcup_{n=1}^{N} W_n(A).$$

Here, we use the notation of $W_n(A)$ to mean the image under W_n of the set A: it is the same as the union of the images of all points in A under W_n. (A set in R^n is bounded

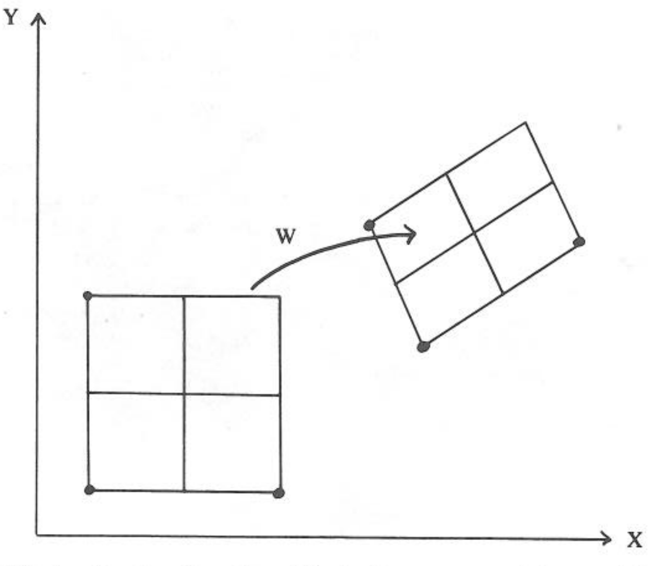


FIGURE 1. An affine transformation will typically map a square into a parallelogram.

if it is contained in an n-dimensional sphere of finite radius. A set in R^n is closed if it contains all its boundary points.) We call A the attractor of the IFS.

An example of an attractor of an IFS is shown in FIGURE 2. It corresponds to six affine maps and is specified by thirty numbers. We draw attention to the following features: (1) The image as a whole is not self-similar—it is not the disjoint union of uniformly shrunken copies of itself. (A magnifying-glass study of the picture will not reveal exact copies of the original.) (2) The image does contain features that recur under affine deformation. For instance, there are various different types of large holes in the image, along with skewed smaller versions of these as well. (3) The image is a

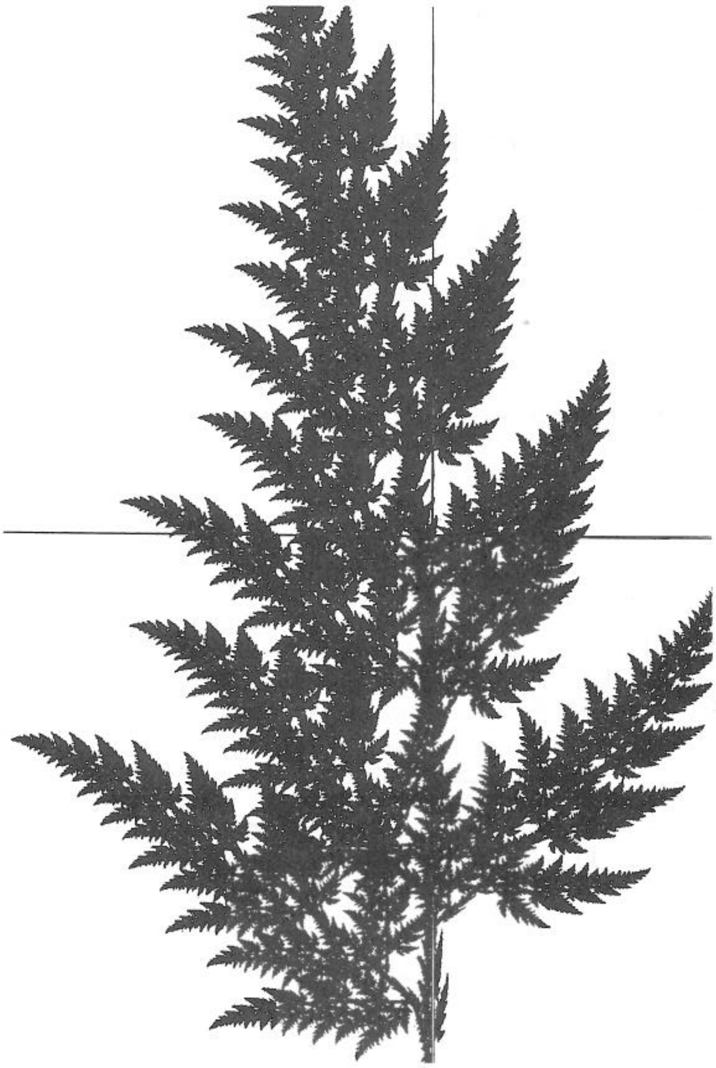


FIGURE 2. An attractor for six affine contraction maps in the plane.

fractal in the sense we defined—it contains features that are not simplified by magnification. (4) The image represents enormous data compression. We treat the set as data on a 1000×1000 grid. Uncompressed, a string of 10^6 zeros and ones is needed to store or transmit the image. Compressed, using an affine IFS, it can be represented exactly by using 30 four-digit numbers, which requires $30 \cdot \ln 1000 = 300$ bits, giving a compression ratio of 3333:1.

We will describe two methods by which the attractor of an IFS may be computed.

These are (1) random iteration an
in K.

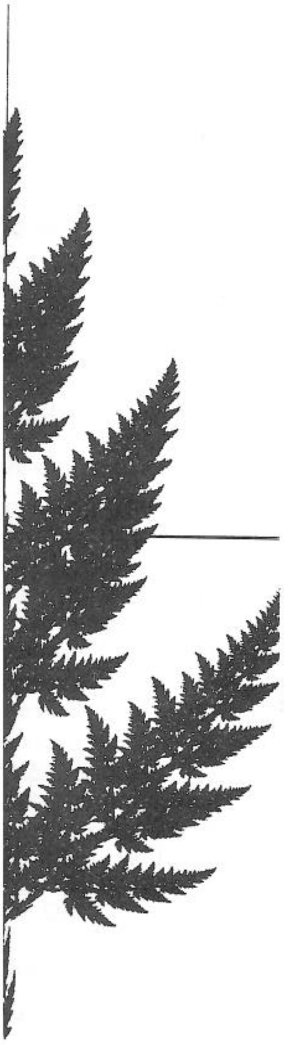
THEOREM ON COMP

Let $\{K, W_1, W_2, \ldots, W_N\}$ be
contractivity factor S (such that
inductively for $n = 0, 1, 2, \ldots$
probability $P_m > 0$ is assigned to th
one might choose $P_1 = P_2 = 0.5$ an
or W_2, is to be applied at each next
points derived from the sequence
Algorithm no. 2: Let A_0 be any no
for $m = 1, 2, 3, \ldots$. Then the s
attractor A of the IFS.

We describe how these algorit
following framework. Let $N = 2$
W_2 take the unit square with co
illustrated in FIGURE 3. We con
graphics screen of resolution 100 b
on this 100 by 100 grid. On apply
that all the x's after a certain num
required, we use the formula

where R is the resolution. In the
Hence, if we choose $x = (0.3, 0.8)$
first seven points, then all of the
Moreover, if we simply plot $\{x_7, x_8,$
in B will have been plotted. If diff
and $P_2 = 0.75$), then exactly the s
may have to plot many more point
of the P's is very small. An incom
is shown in FIGURE 4.

We use the same setting as i
implementation of algorithm no. 2
work directly with the graphics sc
place of the sequence $A_0, A_1, A_2, .$
$B_1, B_2, \ldots$ of the 100 by 100 disc
the grid: for example, B_0 may be th
the notation $B_{m+1} = W(B_m)$ to m
points corresponding to B_m, which
grid. In our framework, we woul
FIGURES 5–14, we show a sequenc
no. 2, starting from B_0 defined by t



action maps in the plane.

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actor of an IFS may be computed.

These are (1) random iteration and (2) set iteration. We use the notation x for a point in K.

THEOREM ON COMPUTING THE ATTRACTOR OF AN IFS

Let $\{K, W_1, W_2, \ldots, W_N\}$ be an IFS where each mapping W_n is contractive with contractivity factor S (such that $0 \leq S < 1$). Algorithm no. 1: Let $x \in k$. Choose inductively for $n = 0, 1, 2, \ldots$, $x_{n+1} \in \{W_1(x_n), W_2(x_n), \ldots, W_N(x_n)\}$, where probability $P_m > 0$ is assigned to the choice $W_m(x_n)$. (For example, in the case of $N = 2$, one might choose $P_1 = P_2 = 0.5$ and use an unbiased coin toss to decide which map, W_1 or W_2, is to be applied at each next step.) Then, with probability one, the limiting set of points derived from the sequence $\{x_0, x_1, x_2, \ldots\}$ will be the attractor A of the IFS. Algorithm no. 2: Let A_0 be any nonempty bounded subset of K. Define $A_m = W(A_{m-1})$ for $m = 1, 2, 3, \ldots$. Then the sequence of sets $\{A_0, A_1, A_2, \ldots\}$ converges to the attractor A of the IFS.

We describe how these algorithms work in computational practice. We choose the following framework. Let $N = 2$ and $S = 0.5$. Suppose that both affine maps W_1 and W_2 take the unit square with corners at (0, 0), (1, 0), (1, 1), (0, 1) into itself, as illustrated in FIGURE 3. We consider the implementation of the algorithms on a graphics screen of resolution 100 by 100 pixels. Let B denote the digitized version of A on this 100 by 100 grid. On applying algorithm no. 1 in this framework, we will find that all the x's after a certain number will lie on B. To find how many iterations H are required, we use the formula

$$S^H = R,$$

where R is the resolution. In the present case, $S = 0.5$, $R = 0.01$, and thus $H < 7$. Hence, if we choose $x = (0.3, 0.8)$ (which lies inside the unit square) and we skip the first seven points, then all of the subsequent points $\{x_7, x_8, x_9, \ldots, x_\infty\}$ will lie on B. Moreover, if we simply plot $\{x_7, x_8, x_9, \ldots, x_{1\times10^6}\}$, then it is very likely that every point in B will have been plotted. If different choices are made for P_1 and P_2 (say, $P_1 = 0.25$ and $P_2 = 0.75$), then exactly the same set B will be obtained in the end; however, one may have to plot many more points before the complete set is plotted, especially if one of the P's is very small. An incomplete rendition of the digitization B of an attractor A is shown in FIGURE 4.

We use the same setting as in the previous paragraph to illustrate the practical implementation of algorithm no. 2. It is convenient (and permissible when $S < 0.5$) to work directly with the graphics screen pixel elements in place of points in the plane. In place of the sequence $A_0, A_1, A_2, \ldots$, we use a corresponding sequence of subsets B_0, $B_1, B_2, \ldots$ of the 100 by 100 discretization grid. Then B_0 is any subset of elements of the grid: for example, B_0 may be the whole grid or just a single element of it. We misuse the notation $B_{m+1} = W(B_m)$ to mean the result of calculating the images of all real points corresponding to B_m, which then projects the result back into the discretization grid. In our framework, we would find $B_7 = B$: moreover, $B_7 = B_8 = B_9 = \ldots$. In FIGURES 5–14, we show a sequence of sets computed using the set iteration algorithm no. 2, starting from B_0 defined by the black square in the upper left corner of FIGURE 5.

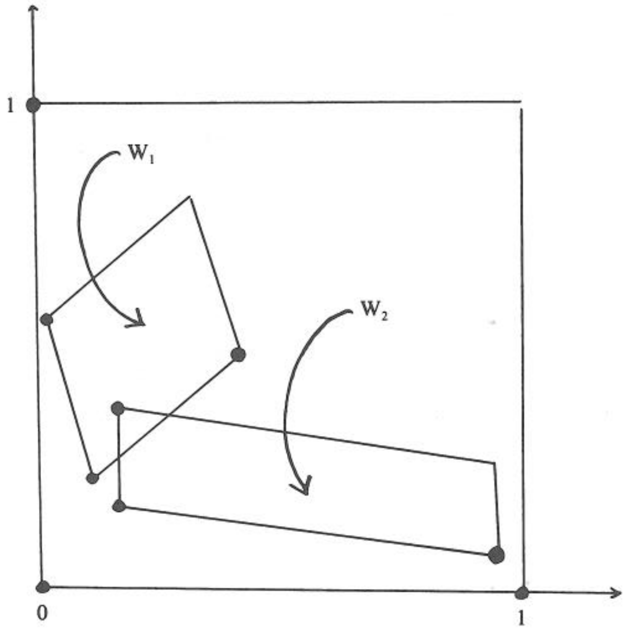


FIGURE 3. Two affine maps that take the unit square into itself.

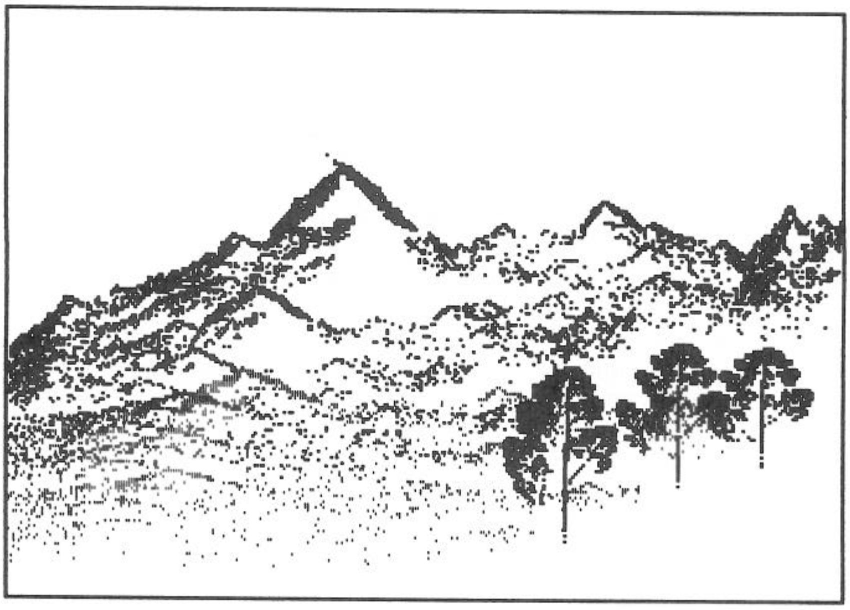
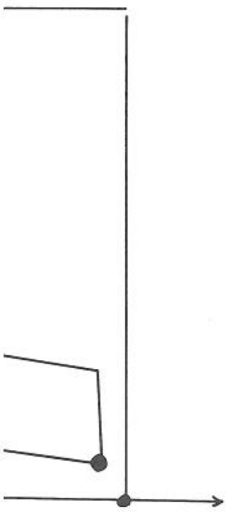


FIGURE 4. A superposition of four incomplete attractors computed using the random iteration algorithm.

FIGURE 5. The following sequence w
iteration algorithm for finding the attr
1000. The black square is B.

FIGURE 6. The set B_1 resulting from a



unit square into itself.

computed using the random iteration

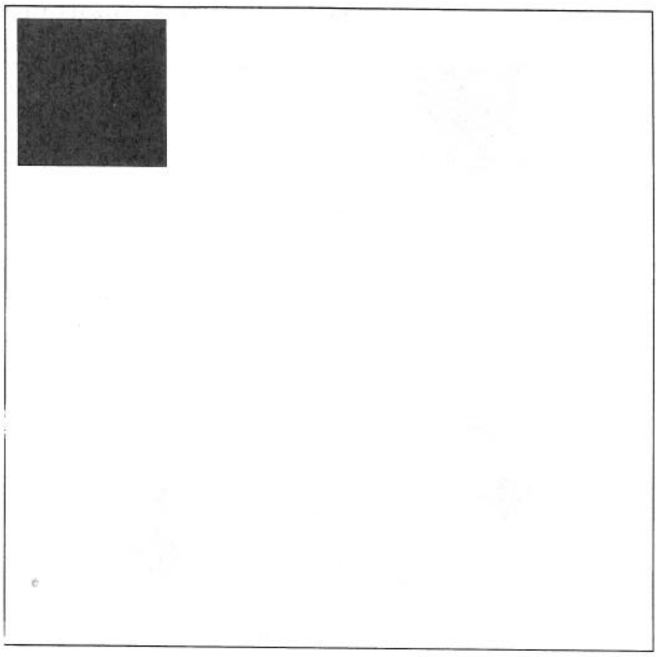


FIGURE 5. The following sequence was computed by Henry Strickland. It illustrates the set iteration algorithm for finding the attractor of a collection of maps. The resolution is 1000 by 1000. The black square is B.

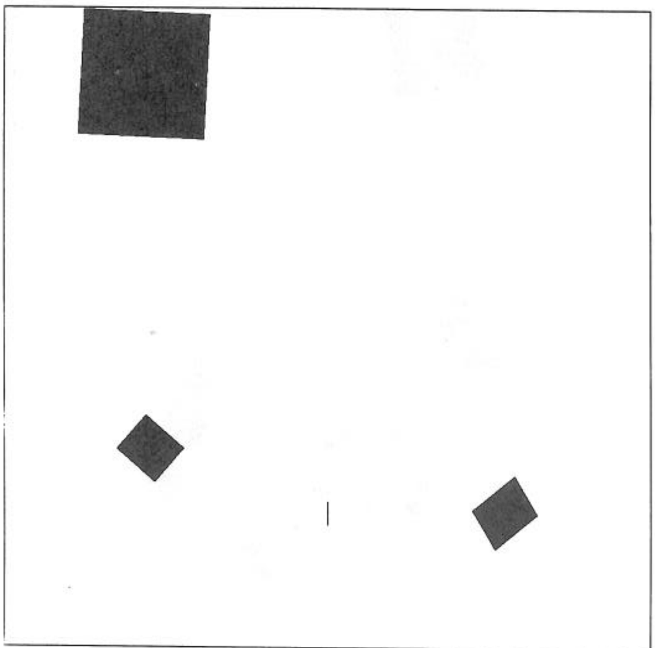


FIGURE 6. The set B_1 resulting from application of four affine maps to the set B_0 in FIGURE 5.

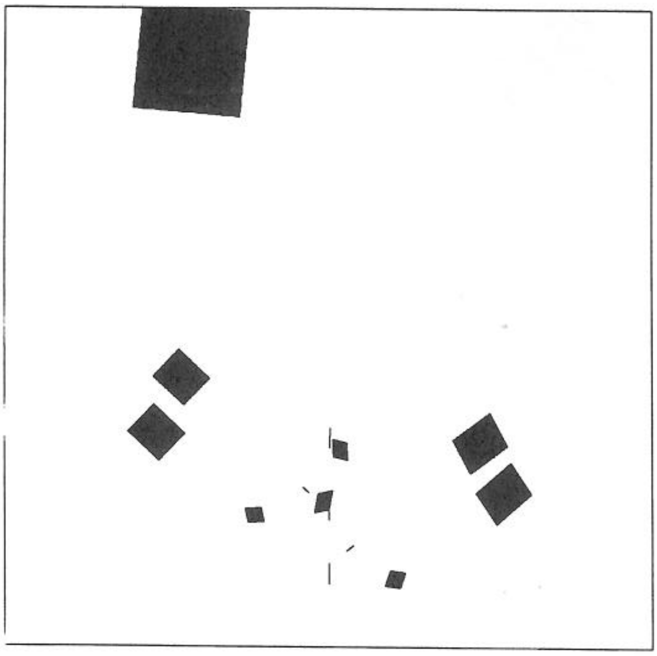


FIGURE 7. The set B_2.

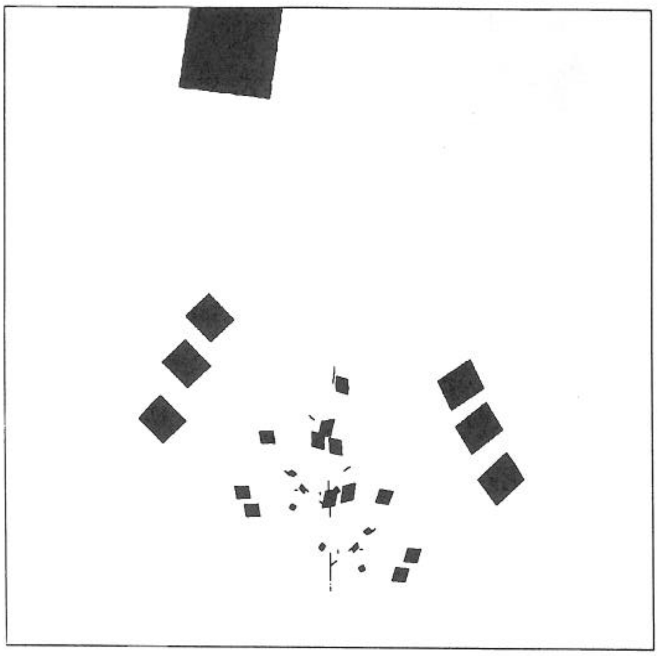
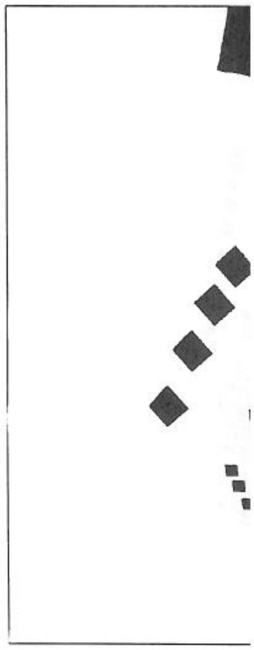


FIGURE 8. The set B_3.



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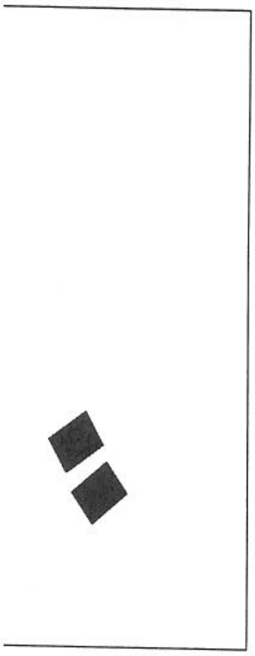
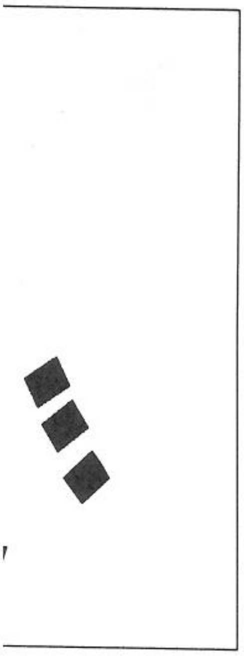


B_2.



$_3$.

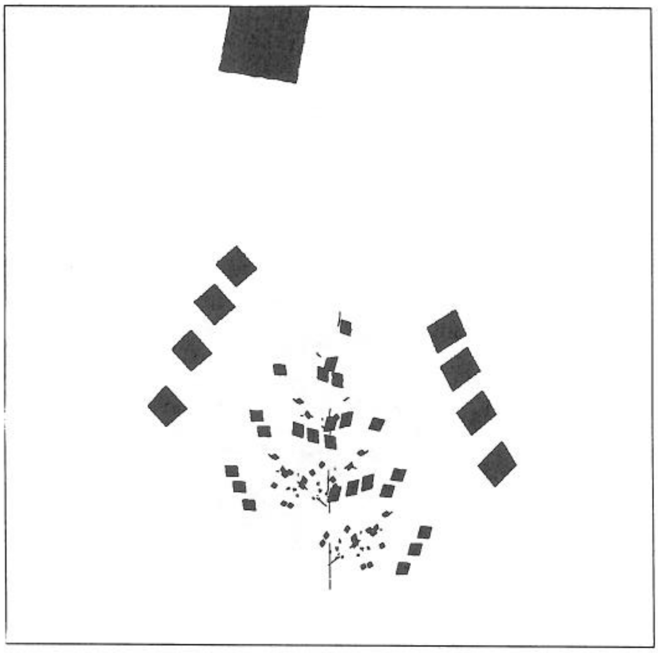


FIGURE 9. The set B_4.

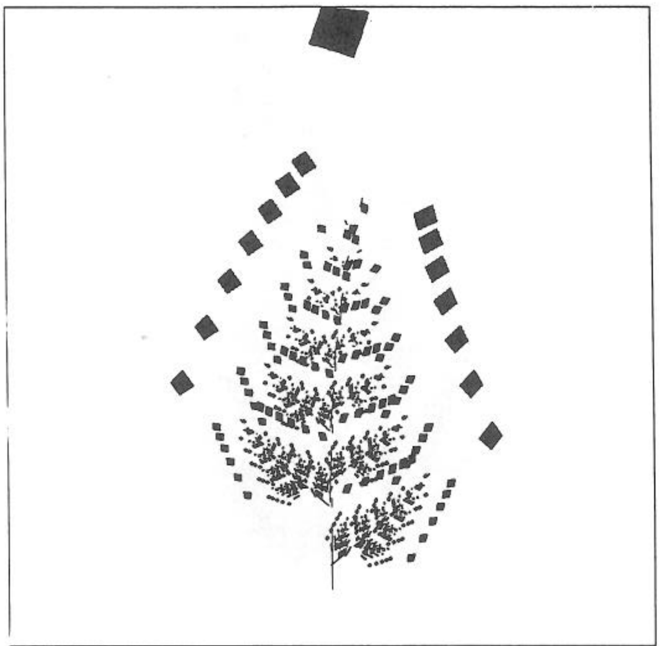


FIGURE 10. The set B_7.

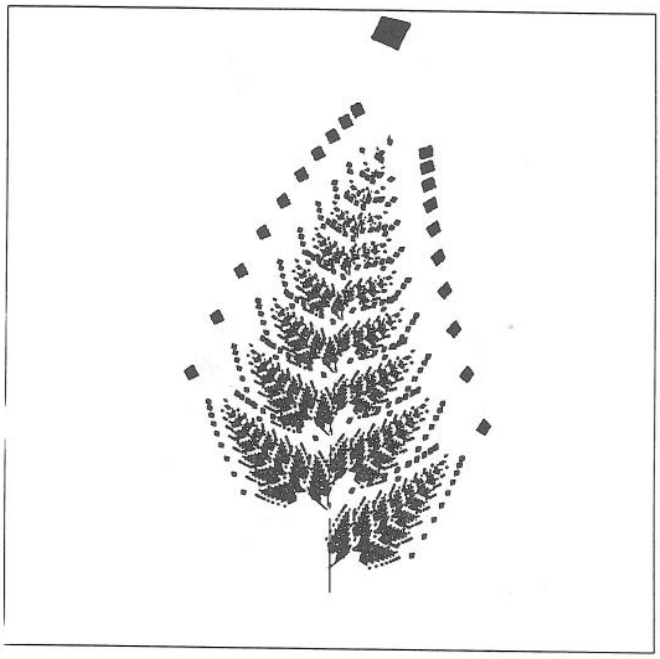


FIGURE 11. The set B_{10}.

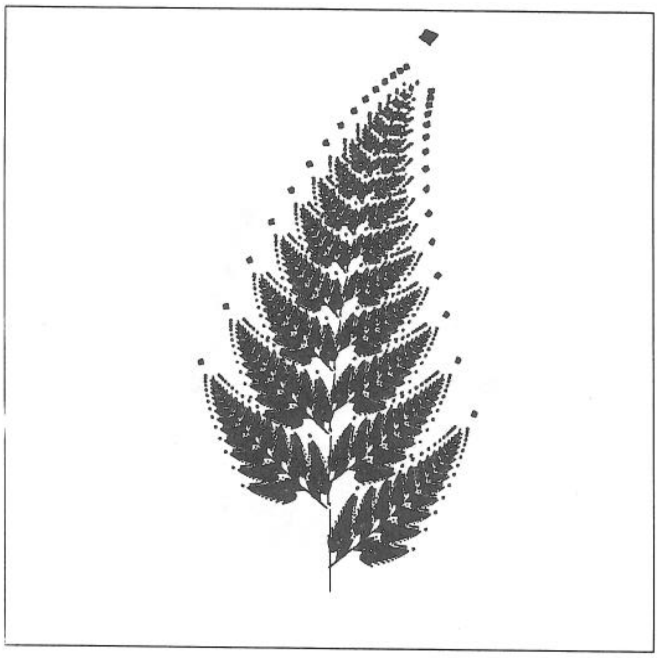


FIGURE 12. The set B_{15}.

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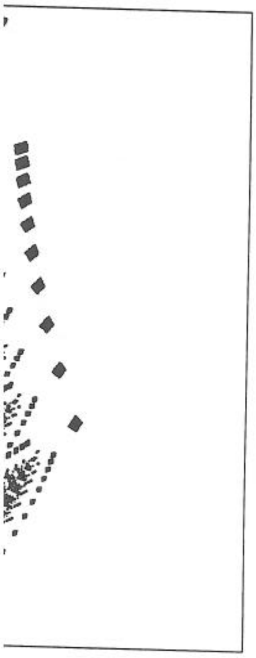
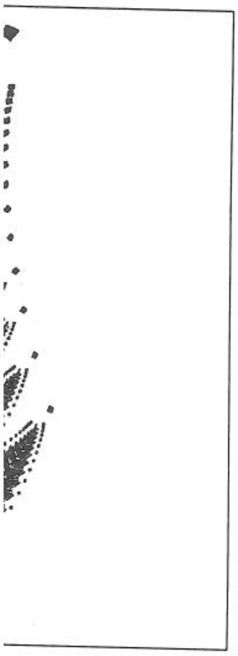


B_{10}.



5.

FIGURE 13. The set B_{20}.

FIGURE 14. The set B_{30}.

This time, there are four affine maps in the IFS. The attractor in this instance is a geometrical model for a branch of a Black Spleenwort Fern.

So far, we have described a way of associating an often elaborate geometrical set with a brief set of numbers that defines an IFS. This is no use as it stands. What one wants is to be able to determine an IFS that represents a given structure. We may want to make a three-dimensional model of the His-Purkinje branching system in the heart in order to make simulations of the timing distribution of the arrivals of electrical pulses at the tips of the structure. To give an idea of how this may be achieved, we consider a simple analogous two-dimensional problem: find an IFS whose attractor approximates the image sketched in FIGURE 18.

First, we need to understand the concept of the distance between two (closed bounded) sets U and V in say R^2. We use the Hausdorff distance $H(U, V)$, which is defined by

$$H(U, V) = \text{MAX}\,\{D(U, V), D(V, U)\},$$

where

$$D(U, V) = \text{MAX}\,\{\text{MIN}\,\{|u - v| : u \in U\} : v \in V\}.$$

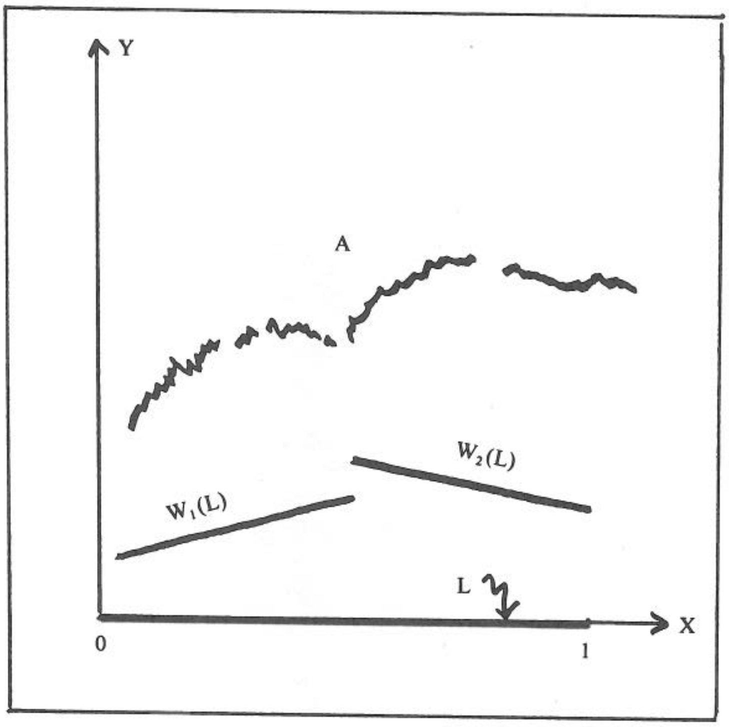


FIGURE 15. A target set L, its images under two affine maps, and the attractor A. As the union of the images moves closer to L, so the attractor moves closer to L. (See also FIGURES 16 and 17.)

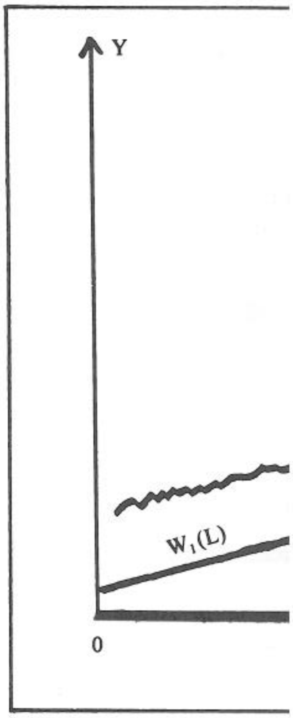


FIGURE 16

For example, let U denote the real i
$0 \le x \le 2$. Then $D(U, V) = 1$, $D(V$
two sets is 2. The important point is
nearly the same set as the Hausdorff
In saying that they are nearly the
resolution.

We can now present the fundam

THEOREM ON FINDIN

Let $\{K, W_1, W_2, \ldots, W_N\}$ be an
contractivity factor S (such that $0 \le$
of K. Suppose that the maps have b
L and the union of the images of L
Hausdorff distance between L and
$E/(1 - S)$. In other words, the clos

We illustrate this theorem with
target set L is the line segment [0, 1
are line segments each of length 0.5

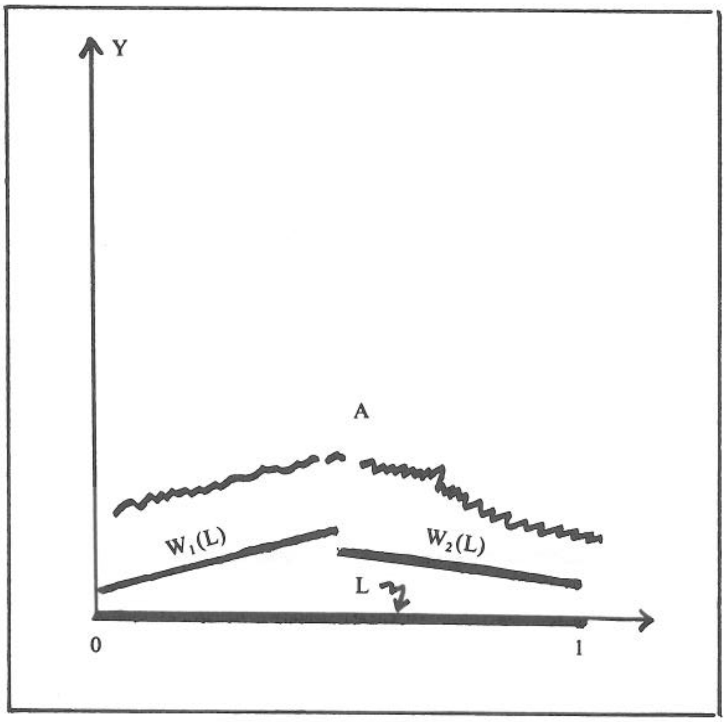


FIGURE 16. See caption to FIGURE 15.

For example, let U denote the real interval $1 \leq x \leq 4$ and let V denote the real interval $0 \leq x \leq 2$. Then $D(U, V) = 1$, $D(V, U) = 2$, and the Hausdorff distance between the two sets is 2. The important point is that two (closed bounded) sets are more and more nearly the same set as the Hausdorff distance between them grows smaller and smaller. In saying that they are nearly the same, we mean that they look alike at a fixed resolution.

We can now present the fundamental modeling tool.

THEOREM ON FINDING THE MAPS (COLLAGE THEOREM)

Let $\{K, W_1, W_2, \ldots, W_N\}$ be an IFS where each mapping W_N is contractive with contractivity factor S (such that $0 \leq S < 1$). Let L be a given (closed bounded) subset of K. Suppose that the maps have been chosen so that the Hausdorff distance between L and the union of the images of L under all of the W_N's is smaller than E. Then, the Hausdorff distance between L and the attractor A of the IFS will be smaller than $E/(1 - S)$. In other words, the closer L is to $\bigcup_N W_N(L)$, the closer A is to L.

We illustrate this theorem with the sketches in FIGURES 15–17. In FIGURE 15, the target set L is the line segment $[0, 1]$, whose images under two affine contractive maps are line segments each of length 0.5; the Hausdorff distance between L and the union

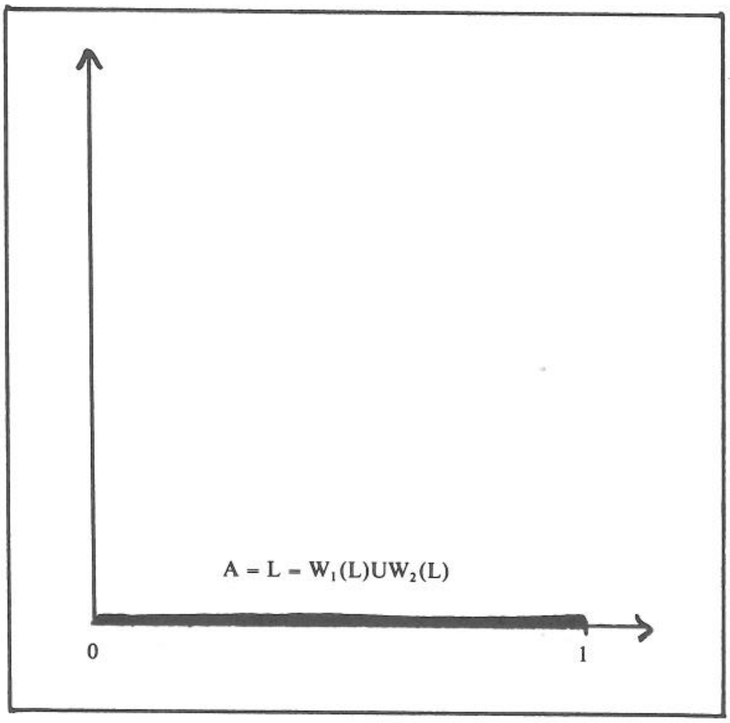


FIGURE 17. See caption to FIGURE 15.

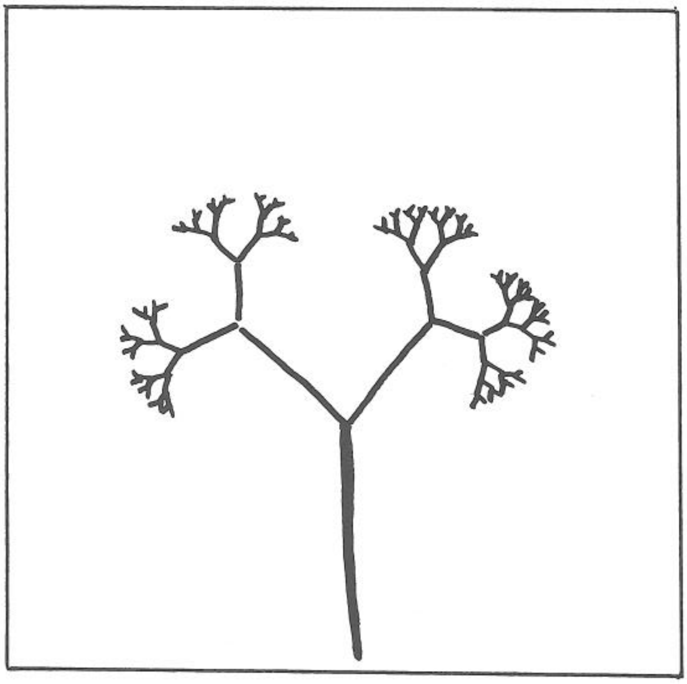


FIGURE 18. A simple branching structure for which one might wish to construct a geometrical model using an IFS of affine contractions.

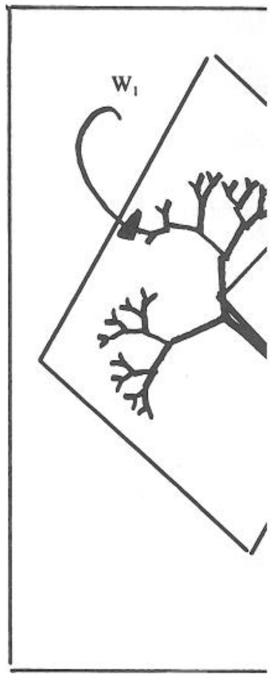


FIGURE 19. This shows how to cho(structure in FIGURE 18.

of its images is about 0.5. The a
distance from L is about 1. In FIGUF
and the attractor is proportionate
indistinguishable both from the u
corresponding IFS.

Finally, we are able to see how
models the branching structure in F
determined by the requirement that
parts shown in FIGURE 19. Althougl
although the image is not exactly th
them, the Collage Theorem assures
for the original target.

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construction of fractals. Proc. R
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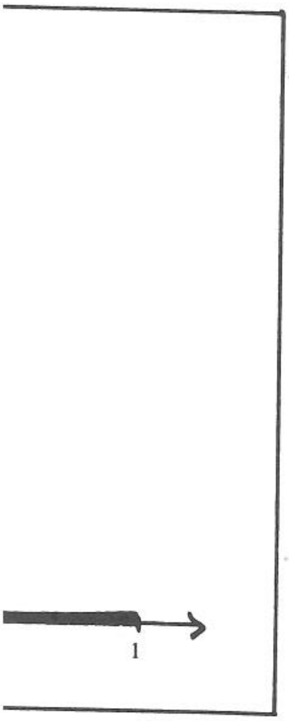
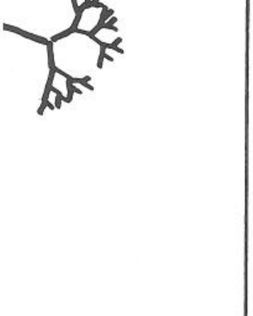


ꟻIGURE 15.



night wish to construct a geometrical

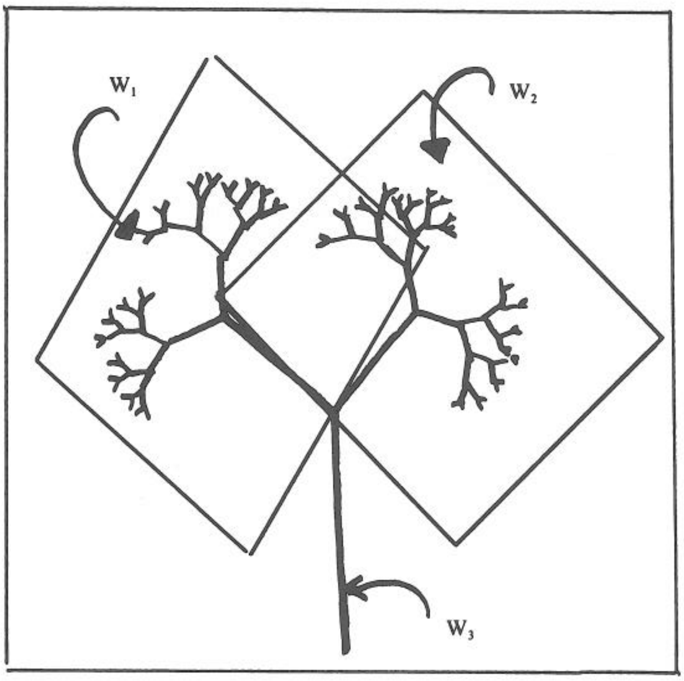


FIGURE 19. This shows how to choose affine maps so that their attractor will model the structure in FIGURE 18.

of its images is about 0.5. The attractor is the squiggly entity and its Hausdorff distance from L is about 1. In FIGURE 16, the images of the line segment are closer to L and the attractor is proportionately closer as well. In FIGURE 17, the target L is indistinguishable both from the union of its images and from the attractor of the corresponding IFS.

Finally, we are able to see how to design an IFS of affine maps whose attractor models the branching structure in FIGURE 18. Three affine maps are required: they are determined by the requirement that they take the whole image to the three component parts shown in FIGURE 19. Although we make errors in the calculation of the maps, and although the image is not exactly the same as the union of the three images of it under them, the Collage Theorem assures us that the attractor should be a reasonable model for the original target.

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What does nonlinear dynamics
normal physiology and elucidating
Over the past few years, in collabora
Mandell), we have been interested i
bedside medicine.[1–11] Although our
soon became clear that the models
applications, and the possibility of ce
suggested. In this paper, we review

The motivation for these inve
questions whose only apparent uni
models. Among these questions wer

(1) What are the mechanisms o
(2) How is a complex structur
does it share any similariti
example, in the lung, the bil
(3) How can one model the abru
certain perturbations, for ex
pacing rate and electrical al
(4) Are there ordering princip
physiologic variables such
subjects and how does one q
(5) Are there new approaches t

While answers to these questic
nonlinear dynamics does suggest ne

[a]This work was supported in part by
Field, California 94035.