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Evolution of an Active Mathematical Theory

Topology started with differential equations; its latest turn brings it back to the differential calculus.

Andrew M. Gleason

It is notoriously difficult to convey a proper impression of the frontiers of mathematics to nonspecialists. Ultimately the difficulty stems from the fact that mathematics is an easier subject than the other sciences. Consequently, many of the important primary problems of the subject—that is, problems which can be understood by an intelligent outsider—have either been solved or carried to a point where an indirect approach is clearly required. The great bulk of pure mathematical research is concerned with secondary, tertiary, or higher-order problems, the very statement of which can hardly be understood until one has mastered a great deal of technical mathematics.

Pure mathematics deals entirely with abstractions. Contrary to popular impression, abstractions are not vague; they can be defined with far greater precision than anything in the real world; consequently, they can support very long chains of logical reasoning. Imagine a biologist who painstakingly studies the digestive process of an amoeba. Suppose, after understanding this to his satisfaction, he retires to his armchair and extrapolates his results through successive levels of the animal kingdom and comes up with a theory of the digestive process in man. It would be absurd to expect that his theory would have any particular relation to the observed facts of human digestion. Yet the mathematician regularly does something rather similar to this. He applies in very complicated contexts theories which were derived in very simple ones, and he not only expects, he finds, that the results are valid, not merely in outline but in detail.

When a mathematician meets a problem he cannot solve, like any other scientist he tries to solve instead some related problem which seems to contain only part of the difficulties of the original. But the mathematician has far more alternatives in choosing a simpler problem than does a chemist or biologist. Other scientists are restricted by nature, whereas the mathematician is restricted only by logical coherence and somewhat vague considerations of taste. Because of this greater freedom, mathematical problems evolve more rapidly, and often the end product seems unrelated to its origins. Yet most of pure mathematics today is concerned with problems that have grown naturally from primary questions of obvious interest, many of which have great practical value. Once one develops a taste for pure mathematics he is likely to pursue his favorite problems without serious concern for their origins. In fact, it is almost necessary to do so, because no one can keep up with all of mathematics today.

This is all very well for the specialist, but to present these problems to the outside world with no description of how they are related to the broader field is a disservice to mathematics. A person may read, for example, that topology is the study of "rubber-sheet-geometry"—that is, of properties of geometrical figures which withstand stretching. Later he reads that a significant theorem of topology has the consequence that at any given moment there are two points on the surface of the earth which are precise antipodes and which enjoy the same barometric pressure and the same temperature. If he now decides that topology is a hopelessly frivolous subject, I cannot blame him.

I should like to give you a brief look at one of the most famous problems of mathematics, the n-body problem, to sketch how some important questions of topology are related to it, and finally to tell you about two important recent discoveries in topology whose significance is only beginning to be appreciated.

Differential Equations

To begin with we must understand something of differential equations.

Suppose the Cleveland police department erected a sign at each street corner in the city which specified that any car arriving at that corner leave along a definite street, no U-turns being permitted. A definite path would thereby be determined for every car. If we knew the traffic directions explicitly, we could compute the path of any car, given its starting point.

An ordinary differential equation presents an analogous problem involving a continuous system of traffic instructions. It specifies a direction at each point of the plane. Imagine a small object moving in the plane and

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always obeying these traffic directions. It will follow a curve in the plane which has the prescribed direction at each of its points. Such a curve is called an *integral* curve of the differential equation. If the instructions are too hodge-podge, it may be impossible to follow them; however, if we assume that the directions specified at nearby points are nearly parallel, we can prove that there is a unique integral curve through each point of the plane. If we imagine all such curves drawn in the plane, then the plane will be paved with curves. In every small area they will look rather like parallel lines, but in large regions different curves may diverge sharply from one another. To solve a differential equation means to find the integral curves explicitly.

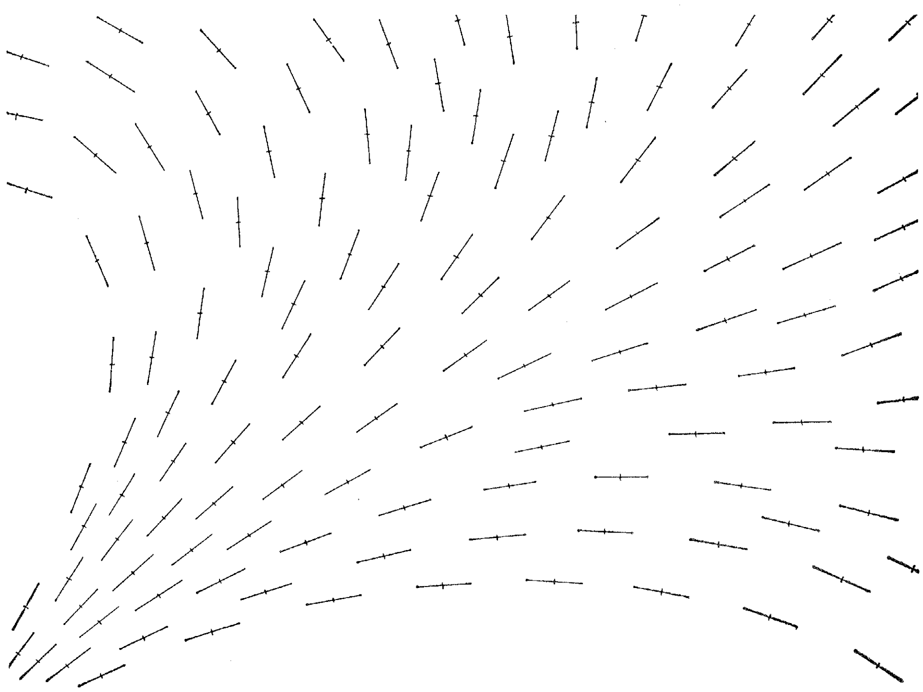


Fig. 1. A first-order ordinary differential equation in one variable. Given directions at each point of the plane, find curves which are at each point tangent to the given line segments.

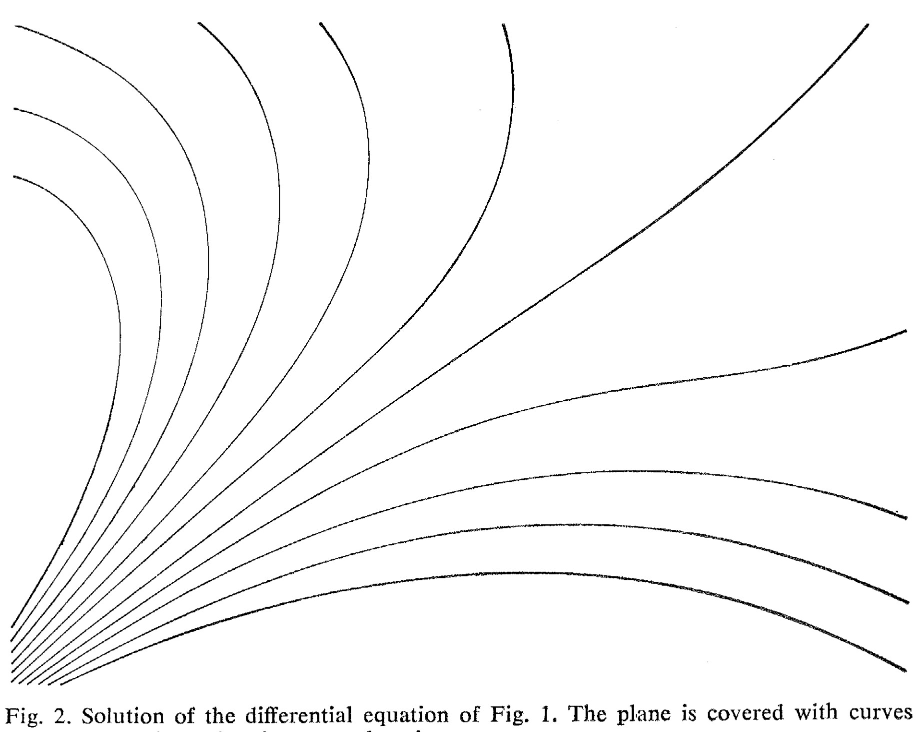


Fig. 2. Solution of the differential equation of Fig. 1. The plane is covered with curves having the desired direction at each point.

A helpful way to think of a differential equation involves the intuitive notion of infinitesimal segments. The direction at each point may be specified by an arbitrarily short line segment through the point (Fig. 1), and we may think of these segments as "infinitely short." These infinitesimal segments are equally infinitesimal segments of the desired curves (Fig. 2), since a curved line looks straight when viewed under sufficient magnification. Thus, the differential equation may be regarded as giving the desired curves fragmented into infinitesimal pieces. The process of reassembling these pieces into whole curves is called *integration*.

Returning to the cars moving in the streets let us suppose that at each street corner, in addition to a direction, a definite speed is prescribed. Then we can not only deduce the path followed by a car, we can also find the exact time required to cover each section of the path.

Correspondingly, in the continuous case we can specify at each point of the plane not only a direction but also a speed. This leads to a new kind of differential equation, in which we assign an arrow at each point of the plane (Fig. 3); the direction of the arrow tells us the direction in which an object should move, and the length of the arrow tells us the speed. An object which moves in accordance with these prescriptions must now not only follow a definite curve in the plane, it must traverse each section of the curve in a definite time. To solve this differential equation we must integrate once to find the paths or integral curves, and then integrate again to find the exact times of flight along the paths.

Generalization to Space

We can, of course, generalize this idea to space. A differential equation is the assignment of an arrow at each point of space. An integral curve of the differential equation is a curve which is tangent at each of its points to the arrow prescribed at that point. If the prescribed arrows do not vary too rapidly from point to point, either in length or in direction, there will be a unique integral curve through each point of space and there will be a unique motion along each integral curve which conforms to the prescribed speeds. To solve the differential equation means to find specifically the integral curves and the times of flight along them.

Take some curve in space, not an integral curve. The various integral curves emanating from this curve will form a surface (Fig. 4). If we start from a system of more or less parallel curves, we will get a system of more or less parallel surfaces. Each of these surfaces will be made up of integral curves. Finding a family of surfaces of this type which pave space nicely is called integrating the differential equation once. With such a family of surfaces explicitly known, we are well along toward solving the problem. Given a point p, we seek the integral curve through p. We know it lies on the unique surface S of our family, which passes through p. Since S is explicitly known, we can confine our attention to S in searching for the integral curve C. Finding C on the (presumably curved) surface S is not very different from finding an integral curve for a differential equation in the plane. The differential equation must be integrated twice more, once to find the curves and again to find the times of flight.

The step to higher dimensions is clear, even if the geometrical imagery has only a fictitious significance. In four dimensions we prescribe an "arrow" at each point. Then we try to find a family of three-dimensional surfaces which "pave" the four-dimensional space; that is, we try to integrate the equation once. If successful, we try to integrate again, which means that we try to "pave" each three-dimensional surface with two-dimensional surfaces. A third integration gives us the integral curves, and a fourth, the times of flight. In still higher dimensions the situation is the same. We successively seek ways to pave space with surfaces of lower and lower dimension, each of which has the property that it is made up of integral curves. After integrating one time less than the original dimension we will have found the curves, and one more integration will be required to find the times of flight along the curves.

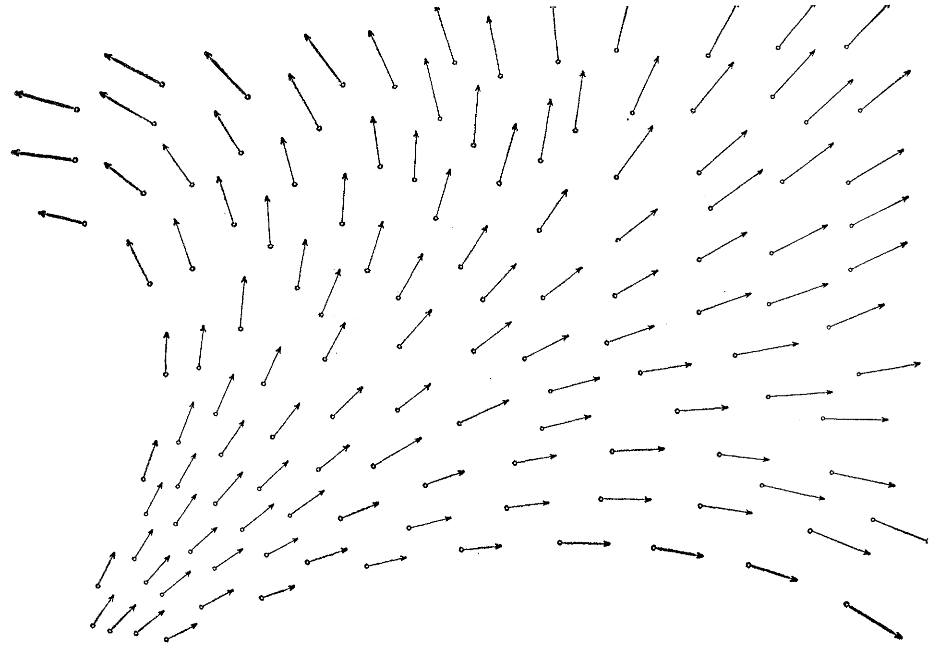


Fig. 3. A parametric ordinary differential equation of the first order in two dimensions. A speed (indicated by the lengths of the arrows) is now prescribed at each point of the plane in addition to the direction specified in Fig. 1. The integral curves are the same as before, but now times of flight along each curve are also determined.

Planetary Motion

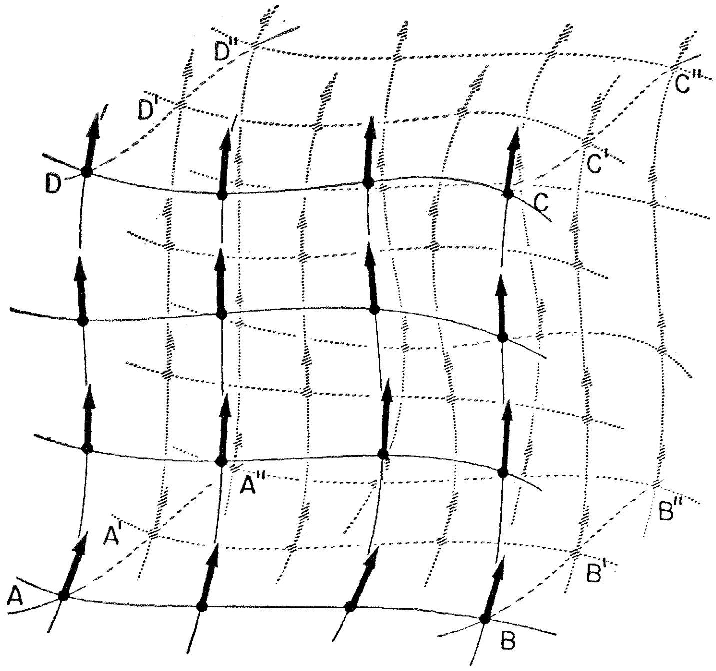
One of the most important applications of differential equations and one of the greatest triumphs of mathematical physics is the Newtonian theory of planetary motion. According to Newton the *state* of each body in the solar system can be described by six numbers, three to designate its position and three to designate its velocity—that is, the speed and direction of its motion.

If we wish to consider an abbreviated solar system consisting of the sun and one planet, we will require six numbers to describe the state of each body, or 12 numbers in all. Thus, the set of all conceivable states of the system can be regarded as points in a 12-dimensional space. At each instant the actual state of the system will be a single point in this state-space. As time elapses, the successive states of the system form a curve in state-space; we can say that the actual state moves in state-space.

Newton proposed that the actual state will move in accordance with a differential equation described by his laws of motion and gravity. These laws prescribe at each point of state-space an arrow which tells the velocity the actual state will have if it should pass through this point. (Since the state of a body includes its velocity, a velocity in state-space is what we ordinarily call an acceleration. Newton's laws of motion and gravity describe the acceleration of each body in the system as a function of the state.) The problem of two bodies is thereby reduced to solving a differential equation. To find the motion of a specific system we must find the integral curve through the starting state and the times of flight along it.

The general problem of two bodies is to find all the integral curves and the times of flight along them. This means we must integrate the differential equation 12 times, once for each dimension of the state-space. This was worked out by Newton, and a remarkable result appeared: the predicted behavior of the planets was in precise agreement with the laws of planetary motion empirically determined by Kepler. As we all know, this theoretical success was one of the great turning points in the history of science.

If we apply the two-body solution separately to the various planets, we are neglecting the interactions between them. The theory also predicts the effect of these interactions. If we take three bodies, the state of the whole system is described by six numbers for each body, so the set of all conceivable states can be regarded as an 18-dimensional space. Again, Newton's theory gives us arrows in the state-space which tell us how the states will evolve. To predict the behavior of a specific system we must find the integral curve through the starting state and the motion along it. To solve the three-body problem means to find all the integral curves and the times of flight along them. To do this, we must integrate 18 times. It is easy to integrate the equation 10 times, leaving 8 to go. We can interpret this as fol-



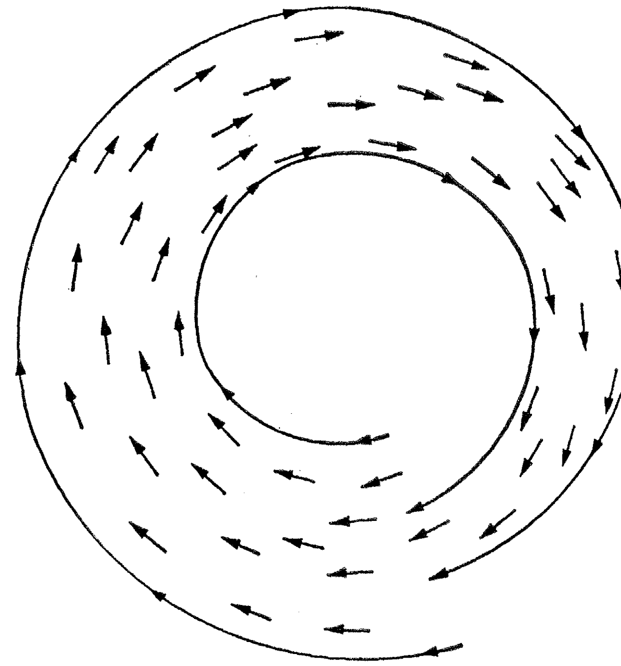


Fig. 4 (left). A parametric ordinary differential equation of the first order in three dimensions. Arrows at each point of space determine the integral curves and the time of flight. The integral curves emanating from the nonintegral curve AB form a surface $ABCD$ called an integral surface. Another curve, $A'B'$, which is more or less parallel to AB, generates another integral surface $A'B'C'D'$ more or less parallel to $ABCD$. Surface $A''B''C''D''$ is similarly generated. This leads to a covering of space by a family of integral surfaces. Another family of curves $AA'A''$, $BB'B''$, and so on, generates another family of integral surfaces. The intersection of two integral surfaces from different families is an integral curve; for example, the integral surface $BB''C''C$ meets $ABCD$ in the integral curve BC. Fig. 5 (right). Parametric differential equation in the plane, with spiral integral curves. Because one curve spirals out and another spirals in, there must be an intermediate one which spirals neither in nor out and is therefore a closed curve. [Courtesy Addison-Wesley, Cambridge, Mass.]

lows. Given a starting state, we can describe an eight-dimensional surface in the space of states such that all future states will lie on this surface. But an eight-dimensional surface is a long way from a curve. From Newton to Poincaré, many mathematicians tried to find further integrals of the three-body problem without success. Finally Poincaré, in the latter part of the last century, showed that there are no further integrals in closed form (*1*). This means that progress can only be made by approximation techniques.

The idea of approximate solutions of the three-body problem, and even of the *n*-body problem, had occupied the minds of mathematicians from the days of Newton. Many of the greatest mathematicians worked to find efficient methods for predicting the planetary motion. Approximate solutions require a great deal of numerical work, and there were no computing machines, not even desk calculators, in 1800. Nevertheless it was possible to predict, even then, the motions of the heavenly bodies within the accuracy of observations.

The theory has served so well that we accept as commonplace the fact that we can predict the exact circumstances of eclipses for many years to come. But on one occasion, at least, a prediction of the Newtonian theory was dramatic. In the early 19th century the observed motion of the planet Uranus (discovered in 1781) was found to be at variance with the Newtonian theory. To resolve the difficulty Adams and Leverrier independently predicted the existence and approximate location of the hitherto unknown planet Neptune, which was found shortly thereafter within 1 degree of the predicted spot!

There have been some major theoretical advances in the Newtonian theory in the last few years. In particular I would like to mention the work of Arnol'd. The solar system appears to be stable. We can predict the course of the planets for thousands of years to come, and we find that they do not stray far from the simple Keplerian orbits calculated by neglecting the planetary interactions. But thousands of years is not forever, and it may be that the solar system is unstable. After several billion years, say, the earth might suddenly emerge from the solar system at a speed sufficient to project it irretrievably into outer space. Or two planets might collide—another form of instability. Arnol'd has proved a strong stability theorem concerning Newtonian *n*-body systems (*2*). Slightly overstated for simplicity, his theorem is as follows. If one body is a great deal larger than all the others and if the system starts in a superficially stable state, then it is in fact stable. Of course this result is of mathematical significance only, because it allows for neither relativistic nor quantum theoretic effects and neglects totally the other stars in the universe.

Topological Methods

Let us return to a special differential equation in two dimensions. Suppose that, as in Fig. 5, there is an integral curve which winds inward and another which spirals outward. It is easy to see, and it can be rigorously proved, that somewhere in between there must be an integral curve which spirals neither in nor out but actually meets itself precisely. Such a curve then continues around and around the same circuit indefinitely. If the differential equation represented a problem in planetary motion, this curve would represent a periodic solution; the system would return at regular intervals to the same state and retrace its motion over and over again.

Note how little we need to know to guarantee the existence of a periodic orbit. In the first place, we don't have to know the inner and outer curves precisely. It is enough to know that one spirals in and the other out. This we may establish through approximate calculation. Secondly, we don't really have to know the differential equation we are dealing with precisely, because a slight change in the equation will leave the same qualitative situation—namely, one integral curve spirals in and the other spirals out.

This is one of the simplest examples of what are called topological arguments. The branch of mathematics which studies them for their own sake is called topology. While some results of topology were known earlier, the subject did not obtain a serious place in mathematics until Poincaré showed that such arguments could prove the existence of periodic solutions in special cases of the three-body problem (*1*). Since that time the subject has grown to be one of the most significant branches of mathematics.

Let us look at another topological fact germane to differential equations. We noted that in solving a three-dimensional differential equation one usually first finds a system of surfaces each of which is made up of integral curves. There will usually be many ways to organize the integral curves into surfaces. It might happen that one of these surfaces is a closed surface—that is, a surface which is finite in extent but without edges. Figure 6 shows some closed surfaces: the surface of a ball, known as the 2-sphere; the surface of a ring or torus; the surface of a two-holed solid. We can go on to the surfaces of solids with more and more holes. This gives us a sequence of surfaces which are all topologically distinct. Furthermore, every closed surface in three-dimensional space is topologically equivalent to one of the surfaces in this infinite sequence of surfaces.

Let us pause to recall what topological equivalence means. It is usually said that topology imagines the figures to be made of rubber and that two figures are equivalent if one can be stretched or compressed without tearing to look like the other. This is not strictly correct. It is permissible to tear the figure, provided you sew it up again along the tear when you are done. This distinction can be appreciated in terms of a knotted and an unknotted loop of string (Fig. 7). These figures are themselves topologically equivalent, but it is quite impossible to deform one to look like the other. To deform the knotted loop into a circle you must temporarily cut it, untie the knot, and rejoin the ends.

Going back to surfaces, we know, then, that if we encounter a closed surface in solving a differential equation in three-dimensional space, it must be topologically one of these. But more than that, it must be a surface which can be covered by a family of more or less parallel curves. A sphere cannot be covered with such a family of curves. Think, for example, of the equator and the circles of latitude on a globe. These cover the sphere neatly except for the poles, where the curves degenerate. It is easy to convince yourself by trials, and it can be rigorously proved, that there is no way to cover a sphere by curves without there being at least one point where the curves break down. In fact, of all the surfaces in our infinite list, only the torus can be covered by curves. Consequently, only the torus can appear as a closed integral surface for a three-dimensional differential equation.

These facts show that topology can provide information of definite value even in applied mathematics. Let us consider some of the questions which arise naturally when we review the facts about surfaces.

The simple sequence of surfaces described in the preceding paragraphs contains every possible kind of closed surface in three-dimensional space. What about non-closed surfaces—that is, surfaces of infinite extent? These are also known, but the classification is quite complicated. What happens if we go to higher dimensions? If we look for two-dimensional closed surfaces in four-dimensional space we find a new infinite list of possibilities. One of these is the famous Klein bottle (Fig. 8), which is improperly displayed in 3-space. It can be put in 3-space only if you let it intersect itself. Of all the new surfaces, only the Klein bottle can be covered with curves, so it is the only new one that might appear in solving a four-dimensional dif-

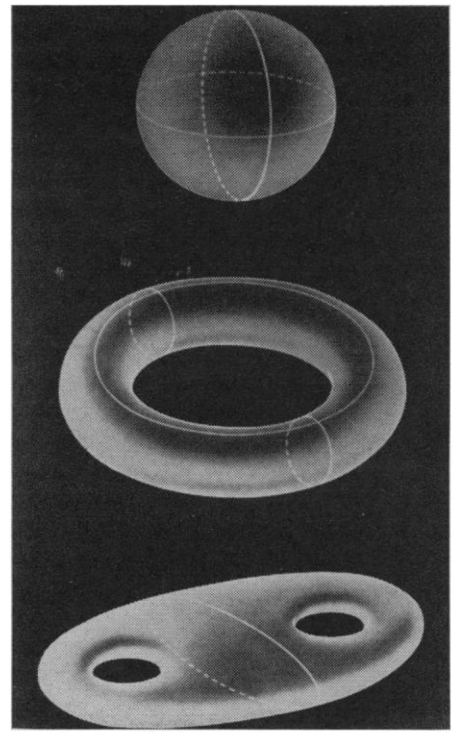


Fig. 6. The simplest closed surfaces in three-dimensional space: (top) the 2-sphere; (middle) the torus; (bottom) the double torus. None of the closed curves shown on the torus or the double torus can be shrunk to a point without leaving the surface. On the other hand, every closed curve in the 2-sphere can be shrunk to a point without leaving the surface. [Courtesy Addison-Wesley, Cambridge, Mass.]

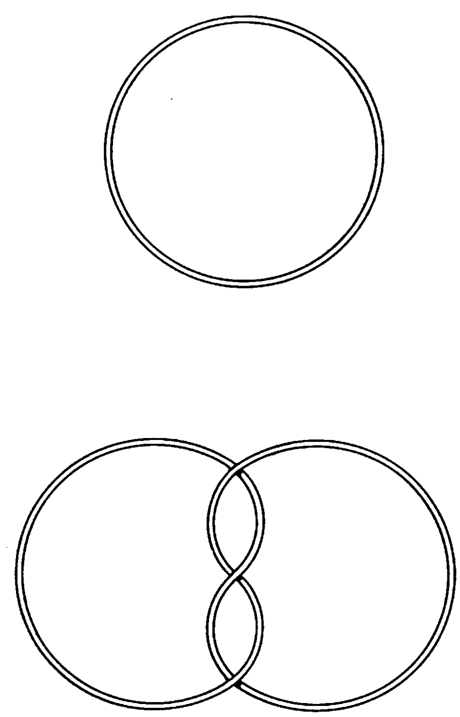


Fig. 7. A knotted loop and an unknotted loop are topologically equivalent, but neither can be deformed into the other unless a temporary cut is made.

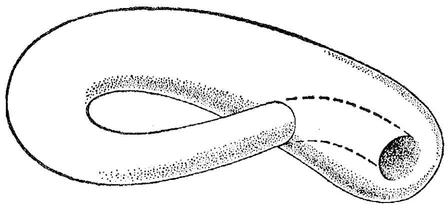


Fig. 8. The Klein bottle is a closed surface which does not fit into ordinary space without self-intersections.

ferential equation. What happens in 5-space? Nothing new. There are no further kinds of closed two-dimensional surfaces in any space.

Suppose we look for three-dimensional surfaces in higher-dimensional space. Can we again find a simple description of all the types? No, or at least not yet. There appears to be an overwhelming number of possibilities.

A truly remarkable problem appears here. The simplest type of closed three-dimensional surface is the 3-sphere. This is the surface of a solid four-dimensional ball. It shares with its relative the 2-sphere the property of being *simply connected*. In everyday terms this means that if you have a loop of string in the surface of a ball you can always gather it in to a point without removing it from the surface. Of all closed two-dimensional surfaces, only the 2-sphere has this property (see Fig. 6). Among closed three-dimensional surfaces the only known simply connected one is the 3-sphere. Poincaré conjectured about 60 years ago that no other closed three-dimensional surface has this property, but this has never been proved [(*3*); since this article was written, proofs have been announced independently, but not yet published, by Poenaru and Haken]. A corresponding problem can be raised concerning spheres of higher dimension. Generally speaking, questions of this sort get harder as dimensions increase. It was a great surprise, therefore, when Stallings in 1960 (*4*) proved that the generalized Poincaré conjecture is true for dimensions 7 and up. His result was extended by Zeeman (*5*) shortly thereafter to cover dimensions 5 and 6.

Among two-dimensional surfaces, only the torus and Klein bottle can be smoothly covered by curves. What higher-dimensional surfaces can be so covered? Even though we don't know all the surfaces, we can decide this question for any explicitly given surface. On the other hand, we have no general method for deciding whether or not an explicit surface of high dimension can be paved with more or less parallel two-dimensional surfaces.

Differential Topology

The latest development in this area is the rise of a new subject called differential topology. It is hard to date its origin, but differential topology can be said to have begun with the work of Thom in the early 1950's (*6*).

Topologists do not distinguish between a square and a circle, because the one can be deformed into the other by stretching. The curves and surfaces which arise in analysis are smooth, like the circle, the sphere, or the torus; they have no corners or edges. Differential topology focuses entirely on these smooth curves and surfaces.

The differential topologist uses a more restrictive notion of equivalence of surfaces than the ordinary topologist. When a differential topologist deforms a smooth surface, he not only keeps it smooth, he keeps every smooth curve lying in that surface smooth. It is easier to describe what he does not do than what he does. Consider an ordinary plane and move it into itself as follows (Fig. 9): every point above a certain line L is kept fixed, but every point below L is moved to the right by an amount equal to its distance below L. Then any smooth curve which crosses L develops a corner after the plane is moved. This is the sort of thing that is prohibited by the differential topologist, although it would be accepted by the ordinary topologist. A differential topologist regards two smooth surfaces as equivalent if the first can be deformed in this more restrictive fashion to look like the second, possibly with some temporary tearing and resewing. The rigorous formulation of these ideas involves the ideas of the differential calculus, and this is what gives the subject its name.

In low dimensions it is true that two smooth surfaces which are topologically equivalent are also equivalent in the sense of differential topology. But in 1955 Milnor gave an example of two seven-dimensional surfaces which are topologically equivalent but not differentially equivalent (*7*). This shows that differential topology is not just topology masquerading in new clothing, it is a genuinely new subject. In another sense, therefore, differential topology began with Milnor's example.

One of the greatest surprises in this now very popular field was found by Kervaire in 1960. He gave an example of a closed ten-dimensional surface with corners which is not topologically equivalent to any smooth surface (*8*).

Let us describe this surface by analogy in the geometric terms of our intuition. Since the figure in question is a surface it can be smoothed out at any point. But no matter how we smooth it, it always has at least one corner. If we smooth out that corner, another one pops up automatically somewhere else.

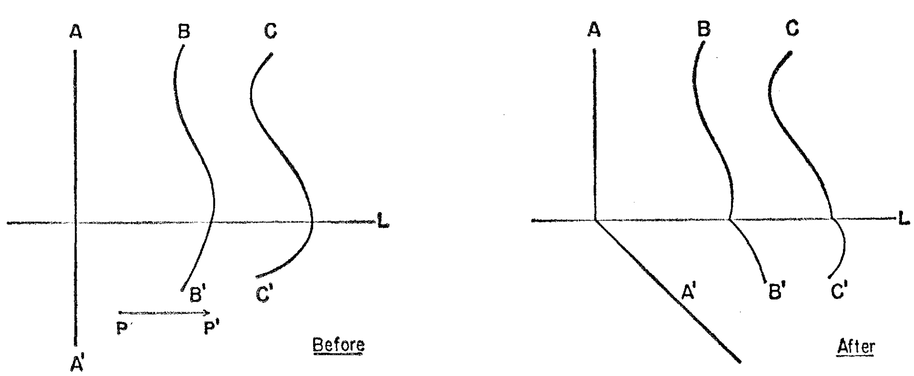


Fig. 9. A motion of the plane into itself which is not admissable in differential topology. Points on and above line L are fixed. Points below L are displaced to the right by an amount equal to their distance below L; for example, P is moved to P'. The effect of this transformation is to introduce corners on the previously smooth curves AA', BB', and CC', at the points where they cross L.

Conclusion

In conclusion, let me point out that I have discussed this general field of mathematics entirely in terms of specific facts and problems. Unfortunately the methods involved in proving these facts involve such a long journey up the ladder of abstraction that it is impossible to give, in any brief article, a fair idea of how they work. Separated from the methods which establish them, facts can convey only a partial picture of mathematics. Like the great temples of some religions, mathematics may be viewed only from the outside by those uninitiated into its mysteries. Anyone who thinks at all about what is involved in asserting that Kervaire's ten-dimensional surface is unsmoothable will sense the power of the methods topologists have developed for organizing our knowledge of space, but understanding these methods is reserved for those who devote years to the study of mathematics.

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The Heterogeneity of the Immune Response

The quantity and nature of antigen can regulate a variety of immunological functions.

Jonathan W. Uhr

The immune response represents a differentiation process in which a small subpopulation of lymphoid cells replicate at an increased rate and synthesize γ-globulin antibodies and perhaps other immune factors. For half a century now several phases of the immune process have been recognized (*1*). First, there is a "latent" period, which is the interval between the first injection of antigen and the commencement of detectable antibody formation. Second, there is the phase of antibody synthesis which lasts for several weeks to many years. Finally, there is the phase of immunological memory, during which there is an enhanced antibody response upon readministration of the specific antigen. This phase of immunological memory usually accompanies antibody synthesis, can occur without it, and usually lasts for years. The enhanced antibody response after reinjection of antigen (the secondary antibody response) has a shorter latent period and a higher peak concentration of serum antibody than the primary response.

During the past decade, there has accumulated considerable new knowledge concerning the cellular and serologic aspects of the immune response. Regarding the cellular aspects, the complexity of the population dynamics of lymphoid cells has become evident. Primary (thymus) and secondary lymphoid organs (lymph nodes, spleen, and so forth) have been described (*2*), and reticuloendothelial cells have been considered necessary for the processing of antigen for the primary antibody response (*3*). It has become apparent that in addition to morphological differences between lymphoid cells, there are striking differences in their response to antigen. Although many lymphocytes encounter antigen in a primary response, only a small fraction of the cells respond by the synthesis of a specific antibody (*4*). There is also a constant exchange of lymphocytes between lymphoid organs and lymph (*5*), and transformation of the small lymphocyte to a large replicating lymphocyte can occur (*5, 6*).

Serologists have long recognized that antibody molecules from the same species and of similar specificity can differ in many ways: size (*7*), avidity (*8*), capacity to fix complement (*9*), ability to cross the placenta (*10*), and others, but there has been difficulty in relating biological to physical properties. During the past several years there have been described three different molecular classes of γ-globulin molecules that can be associated with antibody activity, γ_{1A}, γ_{1M}, and γ_2 as defined by immunoelectrophoresis (*11*), and the biological properties of these molecules are now being systematically studied (*12*). In addition, observations have been made concerning the time of appearance of these classes of antibody during immunization.

This increase in our descriptive knowledge of the cellular and serologic events that follow antigenic stimulation has not yet resulted in an understanding of the mechanisms by which the observed events occur, so at the present time the immune response can only be defined in operational terms. In this article the different immune factors produced in response to antigenic stimulation and the influence of type and dose of antigen on various aspects of the immune response will be described, and the possible modes of regulation of the synthesis of these different immune factors will be discussed.

In these studies, bacteriophage φX174 (φX) has been employed as antigen (*13*) because it presented several advantages over previously used systems. First, the phage is an excellent immunogen and trace amounts (0.1 μg) without the use of adjuvants stimulate the formation of precipitating antibody. Second, the assay for antibody which depends upon the rate of inactivation (k) of phage by a given antiserum is an extremely sensitive and

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