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THE ROLE OF THE CHROMOSOMES IN SEX DETERMINATION

BY

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The subject of sex determination is one which has always intrigued the human mind. The very fact that the offspring of a pair of parents might show only one or the other aspect of sex proved of very vital interest and often-times this interest was a practical one. For those concerned with the succession of royal families, it was very desirable to have male offspring. On the other hand, the breeder of cattle for milk desired to have a preponderance of female individuals. And so each one having any particular concern with this subject conceived his own theory of how it happened that the offspring should be male or female, and because, as a rule, the percentage of males to females was about 50:50, there was an equal chance that the theory might be corrected. And so it happened that among these perhaps hundreds of theories there was an equal measure of truth so far as the results seemed to indicate. Even to the present day we have these empirical theories of sex determination and it seems that the less a person knows about the subject, the more vehement he is in his advocacy of a particular type of explanation. All of the theories may be classified rather briefly into those which assign the determination to the kind of gametes involved, and those which consider the united genes, or zygotes, as the elements of determination.

First, I should like very briefly to review as examples of these empirical theories, some types of them. Up to the beginning of the present century there was no demonstration of the accuracy of any

of the explanations. They were purely theoretical and they depended on some such explanations as this: (1) on the relative potencies of the parents. This was a very favored explanation. There was never any clear definition of the nature of this potency and it varied according to the particular advocate of the theory; but in general the view was held that the more potent of the two parents impressed its sex upon the offspring. That seemed not to be a very good theory because, as a rule, if potency were measured by physical strength, the male was always more potent and yet the offspring appeared in a 50:50 ratio. Nevertheless this was one of the favored theories.

(2) Another one of a somewhat similar nature was that the age of the parents was a determining factor—the older parents impressing its particular sex upon the offspring.

(3) Another great group of theories involved the question of nutrition and these appeared in so many aspects that it is rather difficult to give any review of them. It seemed in many ways to be of perhaps more significance than those others of potency or age. If the zygote received a strong nourishment it might be a male; if the factors of nourishment were weaker, it might be a female. But GEDDES and THOMPSON published a very exhaustive review of the subject of sex determination in the later years of the last century and their general thesis was that the male is anabolic in its metabolism and the female catabolic and they presented many facts to show that the rate of change was greater in the male, whereas the female stored energy and that was especially marked in the difference between the gametes. This book very greatly impressed me and I was interested, in re-reading my own paper on sex determination, to see how very much it had influenced my thinking. In some ways this was unfortunate, because I attempted to associate rather more directly than I should have done, my own ideas with those advocated by GEDDES and THOMPSON.

(4) Another favored explanation related to the freshness or the age of the ovum, and this had some experimental evidence in

favor of it. The HERTWIGS discovered that if frog eggs were fertilized immediately after being laid, a very large proportion of females resulted; whereas if the eggs were kept for a long time before fertilization, the proportion of males was much greater. This was applied to many other very much less obvious cases and became a favored explanation of sex determination.

Some very fantastic theories were devised. One of these was that one ovary produces eggs that result in females, the other, eggs that result in males. There was a corresponding variation of this in that one testis produces sperm that are male-determining, the other sperm that are female-determining. There was an almost infinite number of these theories, or theories of these basic forms, but none of them had experimental evidence or observational evidence of any kind to support them.

It was not until the beginning of this century that we happened upon the real explanation of sex determination, which, as we now know, lies in the nature of the chromosome combinations produced. The beginning of this theory perhaps may be laid to the work of HENKING who, in 1892, observed in the spermatogenesis of the Hemipteron, *Pyrrorchoris*, that there are two kinds of sperm produced. The difference between these two lies in the presence or absence of a chromatin body. HENKING did not definitely identify this chromatin body as a chromosome. Sometimes he called it a nucleolus; sometimes he called it a chromatin body; at other times a chromatoid element; and, again the chromatoid body "X." He did note, however, very definitely, the existence of two types of spermatozoön, the difference between them being due to the presence or absence of this unidentified chromatin element. He offered no suggestion as to the meaning of these two types, so the credit due to HENKING rests only on the observation that there exist in the animal studied, two types of spermatozoa.

About the same time several other investigators, also working on Hemipteran cells, observed bodies similar to HENKING's chromatin

element "X." PAULMIER, working in WILSON's laboratory in Columbia University on the bug, *Anasa*, found what he called a "small chromosome pair," which behaved, he thought, very much like HENKING's chromatin body. PAULMIER erred in his identification of this in thinking of it as a tetrad.

About the same time MONTGOMERY, at the University of Pennsylvania and the Wistar Institute, was working on quite a variety of Hemiptera and he saw this same body which he called a "chromatin nucleolus." He did not note the disposition of this asymmetrically into the two types of sperm and even denied HENKING's observations in this respect, but he did trace the existence of such a body in a large number of Hemipteran species.

My own first paper was published in 1899 on the Locustid *Xiphidium*. It was my first piece of cytological work and I was working quite alone, removed from any large laboratory, and naturally greatly impressed with the authority of those who had previously worked on this subject. But from the beginning I could not conceive the chromatin body which I found, to be in any way related to a nucleolus. It seemed to me always to be definitely a chromosome. Because it was of a different type of behavior from the others and seemed in some way to be accessory to them, I called it the "accessory chromosome." I did not at this time know of HENKING's work and I did not observe the unequal movement of the body into the two types of spermatozoa. This I did not find out until two or three years later. But as soon as I had myself observed the unilateral distribution of the accessory chromosome, it seemed to me that it must be very significant and the argument, as it established itself in my mind, ran something like this:

Assuming that the chromatin is the substance in the cell which has control of its activities, then if we have two types of spermatozoon we should expect to find two kinds of offspring. In search for differences in the members of a species, which would resolve them into two approximately equal groups, there was only the matter of

sexual differences which could be found. Therefore, as a logical conclusion it seemed to me that this element must be concerned in the determination of sex. I presented this theory in a paper, following the title with a question mark—the Accessory Chromosome, sex determinant? That is the history of the case which I will take up more in detail later. Before going into this, perhaps it would be advantageous to have the situation stated, the facts that must be explained.

First we would note that the proportion of males to females is generally 1:1. In very few cases do we find this exact ratio for there may, in some groups, be a few more males in a hundred than females, and in others the reverse situation. Then in the second place we have to note that this normal 1:1 ratio often does not appear. There may be 100% males or 100% females. Our explanations, if correct, must fit all of these cases. In the third place, we have the situation where the species is represented over long periods of time only by females which reproduce, as we say, by parthenogenesis. Then, after a while, these females will produce males, and they will unite with sexual females and produce fertilized eggs. Then we have the peculiar situation where an individual is for a while a male, let us say, and then becomes a female. The same individual at one time of its life is male and at another time female. This is very striking in the case of birds, where sometimes diseases of the ovaries resulting in their destruction will transform a hen which has laid eggs into a rooster which is able to fertilize the eggs of hens. A complete change in the sex of the one individual in such instances has taken place. Then we have many instances of variation in the proportion of the sexes, produced by a variation in external conditions. This may be of many sorts. Many groups of animals are characterized by the existence of individuals which are at one time both male and female—hermaphrodites. Many of the Gastropod molluscs are of this sort. As a rule they are incapable of self-fertilization and they exchange spermatozoa, but they are at one time both male and female.

Then there are instances where one individual has a part of its body with male characters and another part with female characters. Such individuals we call gynandromorphs. These occur, of course, not under normal conditions, but most commonly under experimental conditions. Judging from these experimental cases it is quite possible that they might occur in nature. Then there is a peculiar situation where an individual is neither male nor female, nor a combination of male and female, but something in between—which we call an intersex. These are results of experimental effort, of course. Rarely or never do we find intersexes in nature, although it is quite possible they might occur. The outstanding instance of production of intersexes is the work of GOLDSCHMIDT, who was for a number of years here in Japan collecting various forms of Japanese moths. My first acquaintance with the name Gifu came from hearing a lecture by Dr. GOLDSCHMIDT at Woods Hole. He discovered that by crossing these various races of gypsy moth he could produce all grades between male and female—a complete series of intersexes. He has his own explanation for this. I merely mention this as one of the things we must consider.

It must be admitted from all of these different conditions which I have stated that there can be no such a thing as two kinds of individuals, male and female. By that I mean that male and female are not essentially different things. They are, in reality, only two aspects of one series of characters and that is definitely verified by anatomical studies, where we find that the apparently extreme difference between male and female in a species, is, in reality, only excessive development on one side and corresponding lack of development on the other side of a common series of characters. Sex, then, is not a condition apart from the rest of the organism but is, rather, an expression in one form or another, of a common inherent series of characters in the species. I think it is very important that we realize this, because it is very natural for us to think of the male as being something very different from the female. That is because sometimes the sexes are so very different in their appearance that

taxonomists have placed them in different species. These extremes, however, are connected by all grades, as I have shown, and we must conclude, I think, that we are not dealing with a question of unique characters present in the male, on one hand, and absent in the female on the other. What we have to explain is how a common series of characters can be differentiated in one direction so as to produce those characters which we call male and the same series of characters differentiated in the opposite direction to produce the characteristics of the female. Any explanation of sex must consider all of these different facts. There is one other circumstance which I should perhaps mention, one which is of considerable significance. There are certain insects which are reproduced by polyembryony. That is to say, a single fertilized ovum, instead of producing one individual, may produce two or four or several hundred. In this case all of the individuals are of one sex.

One other interesting circumstance is presented by the free-martin. This is a term applied to an individual, one member of a pair of twins in cattle. This individual, apparently started out to be a female and became transformed in part into a male. In this circumstance the other twin is always a male animal. Dr. F. R. LILLIE observed that in these free-martins the placental circulation of the twins runs together. Instead of remaining separate, the course of the circulation of the two placentae become confluent and the explanation of the production of the free—martin is that the male hormone produced by the male twin circulates in the blood of the female before its hormone has started to develop, and because of this the common series of sexual characters is transformed over into a likeness to the male. It is a very interesting and suggestive case and brings up the question again of balance between the two types of animal with which we have to deal.

Insects appear to have no hormones in their bodies and there the situation must be very different from that in the case of the higher animals like the mammals, where the sexual characters depend upon the circulation of certain substances in the blood. These

substances are called hormones. It is possible to implant a testis in a female animal from which the ovaries have been removed, and thereby to change the characteristics of the female over into those of the male. The substances produced by the testis, circulating in the blood, affect all the characters of the body so as to make them like those of the male, whereas if the natural gonads had remained the animal would have shown the characteristics of the female.

These complicated things we must explain. I should like to go over the situation with regard to the sex chromosomes and explain something more about them.

1. The accessory is a chromosome and not a nucleolus. It seems hardly necessary to mention that in these days, but in the beginning of the work on the sex chromosome this gave rise to most of our difficulties. As I have already indicated to you, MONTGOMERY and HENKING and others who first worked on these structures, thought of them almost entirely as nucleoli. That has always been a puzzle to me. I could not understand it at the time and do not now see why this troubled these able investigators. The only point in which the sex chromosome resembles a nucleolus is that it is a dense and darkly staining body at a certain stage of its development. It does not lie in the interior of the nucleus like a nucleolus, but always on the periphery, and this fact was noted by these investigators and yet they preferred to consider the element a nucleolus.

It was not so very long, however, until it became perfectly evident that the sex chromosome is not a nucleolus, but is, in reality, a true chromosome. At first, because of some striking peculiarities, namely, those which induced investigators to think of it as a nucleolus, led many to regard the sex chromosome as entirely different from the other chromosomes, but it soon developed that that is not the case. The sex chromosome is very much like a real chromosome, or eu-chromosome. It does the same things that they do in its developmental stages. The only difference is that it performs these at a different time and at a different rate from the others—that is, in the male animal where it exists alone. In the female rarely can

it be distinguished from euchromosomes because there it has a mate, as they have, and seems to go through its changes at the same time and at the same rate as the euchromosomes. In the male, where it is unpaired, it has a different history, differing not in character, but in time and degree. We are, therefore, rather thoroughly convinced that the sex chromosome is a chromosome and that it has in the main the same history as the other chromosomes except that in the male it is often unpaired.

In most of the animal and in some of the plant groups which we have studied it is the male that has two kinds of gametes. In the female, there is usually but one. And there are cases, in the birds, for instance, where the reverse is true, where the eggs are of two kinds and the sperm of but one. In most instances, however, the male is digametic, produces two kinds of gametes, and the female unigametic.

There is an important fact to be observed here. This difference is established in the gametes, in the mature germ cells. They are of two kinds. Therefore, even thus early in the development of an individual its potentialities of male and female are pre-determined. The final result, of course, awaits the time of union of the monogametic egg and the digametic spermatozoon. There is choice, as we may say, for the egg between one kind of sperm or the other. There is the same question, of course, as to whether this expression is correct or not, implying selective ability on the part of the egg. Where the result is a 1:1 ratio, it would seem to be entirely a matter of chance, but where the proportion of one sex is very much greater than the other, then it would seem that there must be some selective action, some element of differential attraction or something of that sort, to determine what kind of sperm will enter the egg.

I should like very briefly to sketch for you the history of the sex chromosome in the Orthoptera, so that you may see the basis upon which the theory was formulated. The first observation which I made of this differential element was in the early history of the spermatocytes where, because of its condensed condition and its

peripheral position, and, in the animal observed, its very large size, it was a conspicuous element. I traced this down through the meiotic divisions and found that the element behaved exactly like other chromosomes except that in the first spermatocyte division it did not divide. The result was that in the first spermatocyte division when the tetrads move apart to the poles as dyads, the sex chromosome, instead of dividing, goes as a dyad to one pole of the spindle. The result is to produce two kinds of second spermatocytes, one kind with 12 chromosomes and the other with 11. When these divide they produce each two spermatids and of these, two each have 11 and the other two each have 12.

Why does this chromosome not divide in the first division like the others? We have to go back to the history of the spermatogonial chromosomes to answer that. In the spermatogonia of the short-horned grasshoppers there are 23 chromosomes, 11 pairs plus the unpaired element. If we reduce this to chromatids there are 44 plus two, or 46. Each spermatogonial chromosome is a dyad. In the preparation of the chromosomes for their history in the first spermatocyte, homologous pairs unite to produce tetrads. Two small chromosomes here join two small ones to make a tetrad of small size; two large chromosomes join two large ones to produce a large tetrad. As a rule homologous elements are of the same size and the same shape. These chromosomes have four chromatids and always we note that in the ordinary somatic mitosis, the chromosomes consist of two chromatids each. They simply separate in division and do not again divide. In this case where we have four elements, the four are separated not in one division, but two, and that is obviously why there are two meiotic divisions. That question is one that has long puzzled cytologists. Why should there be two meiotic divisions? At first it was thought that one of these divisions is an ordinary equational division, separating sister chromatids, and the other one a "reduction division" separating the elements which came from the two parents. The reason why there are two divisions, from that standpoint, would be that they are designed to reduce the number

of chromosomes to one half so that in the subsequent fertilization the number is not doubled. That appears to be entirely too simple an explanation. There was nothing to indicate why in order to separate homologous chromosomes there should precede or follow an ordinary equational division. We are very well convinced at the present time that the meiotic divisions are not of this nature. One of them is not merely an equational division and the other an entirely different type of mitotic separation, for we believe now that these two divisions are in reality part of a common process and there are, indeed, cases in which the same chromosome may divide in such a way as to separate homologous elements in the first meiotic division, and at other times may divide so as to separate sister elements. If the theory of crossing-over is true, it is obvious that a single chromosome at one meiotic division divides equationally in part of its length and in the rest of its length segregationally. These two divisions are parts of a common process and the reason we have two divisions is to separate these reconstituted chromatids and distribute them into four separate cells so that if we diagram a particular tetrad on the board and indicate its future history, we would draw four cells and each of the chromatids would go into a separate cell. That, in reality, is what happens in the two meiotic divisions and it is clearly understandable. These elements separate in both divisions, but in the case of the differential chromosome, which has but two chromatids, unless something very unusual happened, it would be impossible for it to divide twice. And in reality it divides but once. In the case of the Orthoptera it does not divide in the first, but in the second division. In the Hemiptera it may reverse this behavior in some species and in others behave as in the Orthoptera. The result is always to produce the two types of spermatozoa, two kinds of cell.

If this is the situation in the spermatogonia we should expect to find what we really do, that there is an odd element present. In the important phase of synapsis this element remains unpaired and that is the time when it is so distinctive. Having no corresponding mate with which to react it becomes condensed early and looks in

some respects like a nucleolus on the periphery of the nucleus. In this circumstance we find the reason for the peculiar behavior of this sex chromosome. In some animals the history of these chromosomes is very clear. In the worm *Ancyracanthus* there are but six chromosomes in the reduced number. One can easily see these chromosomes in the living sperm and it happens that the four resulting spermatids coming from one first spermatocyte remain united. Examination in the living condition reveals that there are two spermatids having six chromosomes and two having but five. There is a plant, *Sphaerocarpus*, in which the conditions are somewhat the same, producing four gametes which remain bound together. In this case two of them are male-producing and two of them female-producing.

I have spoken so far only of the case where the sex chromosome is unpaired. That is the situation in the Orthoptera, but in the Hemiptera there is a different condition. There, instead of the sex chromosome which, in this case, we call X, remaining unpaired, it may have a mate which, for purposes of convenience, is called the Y-chromosome. There the sex elements are, in synapsis, constituted into a tetrad. The Y-chromosome is associated with the X. WILSON studied a large number of Hemipteran species and found that this Y varies in its dimensions from almost an invisible element to a size almost equivalent to that of the X. There appears to be no essential difference, however, in the result of the operation of the sex chromosomes because of the presence of the Y. That would be inferred, of course, from the variable condition of the Y. One curious thing about this Y-chromosome is that it is always retained in the male line. It is sex-limited. It never goes into the female animal, whereas the X-chromosome, on the contrary, passes alternately from the male to the female. In that behavior we may perhaps find an explanation for the peculiar variation in size of the Y-chromosome. As we might expect, it does not show genetical results in most cases. In the forms where it has been most studied it seems to be largely genetically empty, as we might say, but there have been reported cases in the fish, particularly, where certain characters have been

associated with the Y-chromosome. Obviously such association cannot exist in the Hemiptera where it may be present or absent.

That is the cytological situation which we have discovered. It is clearly evident that we have two types of sperm in prevailing cases, and one type of egg. And this directly explains the percentage of males to females as 1:1 in most cases.

Let us consider the application of these facts to the theory. The chromosome theory of sex determination is merely a specific case of the chromosome theory of heredity. That must be obvious from what I have said. As we have discovered from extensive genetical analysis in *Drosophila*, each gene has many effects and one character depends upon the operation of many genes—probably of all the genes. Here is a chromosome which may be definitely identified and its effects noted, and these effects are, as we have observed, to take a common series of characters and on one hand produce out of them the semblance of a male and on the other that of a female. Obviously this chromosome operates in such a way as to alter or modify the action of all the others. If it is present as a single element, one kind of result occurs, but if it is present as a paired element, the opposite result is found. It is, therefore, not directly a sexual element at all. It is not, in itself, a male or a female element. But operating singly, in the presence of the euchromosomes, it produces a male; operating with a mate it produces a female. In view of this it is quite clear that it affects the operation of all the other chromosomes at all stages of development. Only in this way can we account for its effects and I think it must point out the way in which the other chromosomes operate. I anticipate that we will probably get the best understanding of the whole process of differentiation by studying the method by which this particular identifiable chromosome is able to so modify and influence the action of all the others as to produce the sexual differences. Because, after all, this question of sex characters is merely one aspect of the general one of how all the structures of the body are produced out of a single cell by the processes of development and differentiation. That, as you know,

is the great unsolved problem of biology. We can tell precisely what genetical results we may get out of a known combination of characters; but we do not know a single thing of the processes by which a single egg subdivides into millions and billions and trillions of cells so as to produce the end results which are exactly those which we should anticipate in the light of previous experience. This question of sex determination takes its place then, as part of that great problem of differentiation in development.

The theory of sex determination has in the years of this century developed side by side with the whole theory of heredity and has continued a part of the chromosome theory of heredity as it started out to be. It is a logical conclusion drawn from the facts, not a conscious search for the explanation of inheritance. I had no thought whatever of sex nor determination of sex in my studies on the spermatogenesis of the grasshopper. I encountered this peculiar chromosome and had to explain the unusual activities which it showed. And there was but one logical conclusion—the theory of sex determination, which presented itself as the only one which might be drawn. I think because it developed in this way it was perhaps stronger than if it were evolved especially as an explanation of the whole question. It was one incidental element in the whole problem of correlating the behavior of the chromosomes with the behavior of characters in organisms. It was the first definite association between a particular chromosome and known characters in the body. Naturally at first a direct relationship seemed to suggest itself. As I have told you, this was my very earliest work and I had no opportunity to confer with others or to read much of the literature. And so, having read all that I could and found that there were no references anywhere to chromosomes of this character in the female, I naturally concluded that they were not there. I found many references which seemed to indicate that investigators had seen sex chromosomes in the male. So it was the one conclusion possible at that time that this particular chromosome, being found in the male, was restricted to the male and was therefore directly a male-

determining element. I have thought this over often since and it seems to me that, presented with the same situation now, I should be forced to the same conclusion. It turned out to be just the opposite of what I had supposed. The reason why there had been no observations of such chromosomes in the female is that there the elements are paired and behave almost exactly like the other chromosomes. At almost the same time WILSON and Miss STEVENS, working independently, found that the female possesses one more chromosome instead of one less. It immediately appeared that the simple explanation which had suggested itself to me was not the correct one. We made the same mistake in assuming this direct connection between Mendelian so-called "unit" characters and particular genes. This very simple relation seems never to obtain in living matter. We are, in reality, always dealing with a very complex situation, one in which a definite factor is not simple in its effect. It does not, for instance, operate only at a particular time so as to produce one result, but it is a part of all the integrated factors, a reaction system in which all the elements are operating all the time, and the extremely complicated result is due to this constant action and interaction between these final elements of control, the genes or biophores, or whatever they may be called.

At the same time that I was working on this problem, my first graduate student, Dr. SUTTON, was studying with me the behavior of the chromosomes in the spermatogonia of the grasshopper. He went the next year to Columbia University to work with Professor WILSON and had hardly settle down to work there when BATESON came from England, and explained MENDEL's work for the first time. Immediately the explanation of alternative inheritance of characters suggested itself to SUTTON because we had already discovered that the chromosome complex of Orthoptera consists of 11 pairs and a single chromosome. An explanation was thus afforded to exactly correspond to the behavior of chromosomes in meiosis and fertilization. A specific understanding of the sex-determining function of a particular

chromosome at once took its place in this larger and more comprehensive view of the whole problem of heredity.

I have told you that the relation is not immediate and direct between this particular chromosome and the sex characters. It is not that this is a male element and something else a female element, but that it has certain powers which, in relation with those of the other chromosomes, results in producing a male animal when it is single, and a female when there are two. It would logically follow, if this is correct, that the source of this chromosome is immaterial. It is not that it comes in with the spermatozoon that it is male-producing. It has been found experimentally that it makes no difference whether this particular chromosome comes in with the spermatozoon or whether it is supplied by the egg itself. There are cases where two X-chromosomes of the egg are not separated; they remain in the egg. In that event, fertilization by a spermatozoon which would ordinarily produce a male, produces a female. It is the presence of two sex chromosomes which is responsible for the development of female characters, and it makes no difference whether these both come from the female or whether one is derived from the male. This has been lately developed further by the work of BRIDGES and it appears therefrom that if cell balance is altered

Autosomes plus XX — female
 „ „ X — male

between the set of euchromosomes and one or two of the sex chromosomes, the results are modified. However, if there are the same proportions of autosomes to sex chromosomes, the result will be the same proportion of maleness and femaleness. In this same way, supermales or superfemales or intersexes between these two may be produced. It is very clear that the sex of an individual depends upon the balance between the sex chromosomes and the other chromosomes. It is not, I think, as WILSON and MONTGOMERY suggested, that two doses of X means a female and one a male. It is not so simple and direct as that. It is a question of the interrelation of all the

euchromosomes on one side and the sex chromosomes on the other that produces male and female and that, as I believe, must represent the whole situation with regard to the development of the structures in the body which we call characters. They are determined by the action and interaction of the whole set of chromosomes with this differential element as determiner of the sexual inclination of the individual.

Perhaps it might be interesting to examine into the explanation of the unusual forms of sex relation which I have mentioned. Take, for instance, the gynandromorphs. Sometimes these are male on one side and female on the other, or we may have a mosaic pattern of cells in the body, neighboring cells being on one hand male and on the other hand female. This is easily understood of course in the case of insects where it most commonly occurs. When we study these cells we find that if they show the characters of maleness they have one sex chromosome; if they show the characters of femaleness, they have two. There are no hormones to affect the situation. It makes no difference in neighboring cells, and it has been easily explained how one half of an animal is male and one half female. An immediate and direct relation between the sex chromosomes and the character of the cell often has been discovered in these mosaic animals.

In the case of parthenogenesis which was first suggested as being absolute refutation of the theory of sex determination by chromosomes, we find, on the contrary, that it supports the theory exactly, in the behavior of the chromosomes in the successive generations of animals that reproduce by parthenogenesis, because there the sex chromosomes are retained in the spermatozoön so that always when the egg is fertilized it produces a female; and later when males are produced by this series of parthenogenetic females, one chromosome is thrust out and the number reduced by one. So that the cases of parthenogenesis fall directly into line and afford a strong support of the theory of sex determination by these particular chromosomes.

The case of intersexes is not so easy. These occur only in the laboratory, so far as they have been carefully studied. In this case the eggs are dimorphic. All we know is that we can get a whole series of intergrades by taking the sperm cells from different kinds of parents. We have, as I have told you, good reason for believing that the sex characters are the result of interaction of these particular chromosomes with others. So it is not strange, perhaps, that if we take chromosomes from another species and bring them in, the degree of this interaction should be different. GOLDSCHMIDT has explained all of his intersexes by assuming certain numerical values of the sex power of these chromosomes. By putting it mathematically he has evaluated all the intersexes which he produces. That is only another way of stating the facts. Assigning numbers to them does nothing more than to say, as I have said, that the power of chromosomes derived from one species may differ from that derived from another. It is only a matter of convenience.

I might go on at considerably greater length without, perhaps, doing anything more than to complicate the subject. I have tried to point out to you the course of the investigations which have led to the present conception of the specific action of these chromosomes, and I think probably there is no other biological theory that is now better founded than this, especially when we regard the action of the sex chromosomes as indicative of the action of all chromosomes. Whatever evidence supports the chromosome theory of heredity directly supports the theory of sex determination by means of chromosomes and anything that militates against the general theory of heredity as influenced by chromosomes, directly affects that of sex determination by these particular chromosomes. This is just a specific instance of the whole theory of heredity depending upon the action of chromosomes.
