SEX DETERMINATION

F. A. E. CREW

METHUEN'S MONOGRAPHS ON BIOLOGICAL SUBJECTS

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PREFACE

THE purpose of this book is to present the salient facts relating to sex-determination and to guide the student to further reading. It presupposes that the reader already has a fair knowledge of genetics and cytology; it restricts itself to a consideration of the cytological and genetical aspects of sex-determination and does not consider the problems that cluster round the actual development of the sexual characters, since such development pertains not to sex-determination but rather to sex-differentiation.

Those who wish to explore more fully the matters touched upon in this book are advised to turn to *Advances in Genetics*, edited by M. Demerec, four volumes of which have been published so far in 1947–1951 by Academic Press Incorporated, New York, and to *The Evolution of Genetic Systems* by C. D. Darlington, published in 1946 by the Cambridge University Press. Such as wish to proceed from a study of sex-determination to one of sex-differentiation can profitably refer to F. H. A. Marshall's *Physiology of Reproduction*, third edition, edited by A. S. Parkes and published in 1952 by Longmans, Green, London, or to *Sex and Internal Secretions*, edited by Edgar Allen and published in 1939 by Williams and Wilkins Company, Baltimore.

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CHAPTER I

THE GENETIC THEORY OF SEX-DETERMINATION

Sex (L. *seco*, to cut), the distinction between male and female, the property by which an individual is male or female. Sexuality, the quality of being distinguished by sex.

FROM the very beginning of human existence a difference between the two contrasted types we know as male and female respectively must have been recognized. Within every individual the force of sexuality has operated to focus thought upon matters sexual and to yield an intense awareness of the sexually contrasted form. It can safely be assumed that this observed difference in mankind and in the animals man domesticated has at all times intrigued the human mind and provoked speculation concerning its significance and causation. Every individual displays the property of sexuality and by his own experience knows of it. Speculation concerning it has never been restricted to students of biology; any man can claim to be his own authority.

The observations that required an explanation were but few to begin with. Maleness and femaleness were attributes which were exercised in the sexual relationship. The sexual union of male and female resulted in reproduction, in the production of offspring among whom males and females appeared in more or less equal numbers. In this production by a male and a female of males and females there was to be observed an orderliness and a precision which suggested that some relatively simple mechanism was involved.

Hypotheses concerning the way in which and the time during the life history of the individual at which sex is determined have been plentiful. For the most part they were elaborated at a time when little or nothing was known of the anatomy and physiology of the cell, of cell division, of gametogenesis and of fertilization, or they were constructed by such as were unaware of, or chose to disregard, what was

known concerning these matters. Up to the beginning of the present century each of them in its turn was destroyed when it proved to be incapable of accommodating some new observation. In retrospect it is easy to understand how it came about that a theory derived from and based upon the experience of an obstetrician, for example, could not be stretched to include the outcome of the experience of a breeder of habitually polytocous livestock.

Then, as the studies of the zoologist and of the botanist widened to include an ever-expanding number of species, it is understandable how it happened that a theory elaborated by a zoologist proved to be of no value whatsoever to a botanist who had encountered in his material phenomena strongly resembling those of sexuality in the animal. That for which men continually sought was a theory that could accommodate all that was known about the phenomenon of sexuality wherever it appeared, and as this knowledge expanded the difficulties of constructing a satisfactory theory of the causation of sex multiplied.

Each of these theories of sex-determination has to be examined against the background of the total biological knowledge that was in man's possession at the time when the theory was promulgated. If it accommodated all the observations thus far made, and if it was a reasonable, intelligent groping after understanding, then in its day it was a good and useful theory. That it is now unwarrantable in the light of our vastly increased knowledge of matters biological in no way robs the theory of its merit.

By the beginning of this century our knowledge of the cell, of gametogenesis and of fertilization had become greatly expanded, and in the earliest years of the century, as an outcome of the confirmation of the Mendelian theory of organic inheritance, much attention became focused upon the mode of transmission of inherited characters and the search began for the actual mechanism of segregation that was postulated by the Mendelian theory. Thus it was that the sciences of genetics and of cytology entered into a phase of intensely active development.

The facts to be accommodated by a theory of sex-

determination could now be stated more exactly. In a wide variety of species sex-dimorphism occurs; within them there are males and females. Sexual reproduction, taking the form of the fusion, permanently or temporarily, of two complete individuals or parts thereof or in the union of single cells derived from one and the same individual or from two individuals, occurs in all those groups of organisms in which the presence of a nucleus has been demonstrated. In the higher forms sexual reproduction consists in the formation of single cells, the gametes, the separation of these from the rest of the individual and their subsequent fusion in pairs to form the zygotes, the new individuals of a new generation. In most of these forms two kinds of gametes are to be found—a small, active, motile gamete elaborated by the male (or by the testis of the hermaphrodite) and a relatively large, inactive, non-motile gamete elaborated by the female (or by the ovary of the hermaphrodite). These gametes constitute the only organic bridge connecting the generations.

Usually during spermatogenesis the nucleus and the cytoplasm of a cell are equally divided among four functional spermatozoa, whilst during oogenesis three of the products of division are suppressed and extruded to become the polar bodies, only one remaining to become the functional ovum.

The simplest form of spermatozoon consists of four parts: (1) the nucleus forming the head; (2) the centrosome, a non-nuclear body forming the middle piece from which the axial filament of the vibratile tail is developed; (3) the mitochondria, bodies of non-nuclear origin which form the sheath of this filament, and (4) ordinary cytoplasm which forms a thin coat over the head and tail. The nucleus alone is the constant constituent of the spermatozoon; it alone fuses with the nucleus of the ovum. No other organ save the centrosome takes any part in the development of the new individual.

The essential feature of sexuality is the production of two different kinds of gametes by the individuals of a species, male-type by the male, female-type by the female. Fusion between gametes is restricted to such as possess and display

contrasted characters (details of structure and of behaviour), and usually to such as are derived from two sexually contrasted individuals.

The division of a cell into two by simple fission is no mere casual cleavage; it is a process of precision, karyokinesis or mitosis, the essential feature of which is the exact halving of the two chief constituents of the cell, the nucleus and the cytoplasm, so that the two daughter cells that result are, save in respect of initial size, exact copies of the cell that produced them.

The most striking features of mitosis are the exact and precise division of the chromosomes and the precise distribution of the daughter chromosomes so formed. In respect of their chromosome constitution the daughter cells are exact copies of the mother cell that produced them.

In each and every species there is a characteristic number of chromosomes within the nuclei of its component cells. For example, man has forty-eight (Evans and Swezy, 1929). These exist in the form of pairs, the members of any given pair (with one exception later to be considered) being alike in size, shape and behaviour during cell-division.

This constancy of the chromosome number could not exist if at fertilization both the egg and the sperm brought into the new zygote that number of chromosomes which is characteristic of the species. Offspring have the same number as the parents (polymitotic forms and polyploidy being disregarded). Constancy is maintained by a reduction of the chromosome number to a half during gametogenesis. The existence of this process was postulated by Weismann (1887). His hypothesis has been verified universally since then. Wherever there is fertilization there is also reduction, which in essence consists of two divisions of the nucleus of the cell associated with one division of its chromosomes, with the result that four daughter nuclei are produced, each of these having half the number (the haploid number) of chromosomes characteristic of the species. Meiosis, this process of reduction, is a modification of mitosis.

Fertilization consists essentially in the bringing together of two half-sets of chromosomes and the consequent re-

establishment of the characteristic chromosome number. One member of each of the pairs of chromosomes with which the new individual is endowed comes by way of the spermatozoon from the father; its mate comes by way of the ovum from the mother.

Many of the details of structure and function that are exhibited by the individual are the expression of the hereditary constitution of the individual. Mendel postulated that such characters were brought into being by the action of 'hereditary factors'. In every individual's constitution, and in respect of any given character, there were two such factors, only one of which passed into each gamete. Commonly, of the pair of hereditary factors one was dominant, the other recessive, the dominant one alone exerting an influence during development. Thus an individual exhibiting the dominant member of a contrasted pair of hereditary characters could be either a homozygous dominant (DD) or else a heterozygous dominant (Dd).

Mendel (1865) himself hazarded the suggestion that sex-determination might prove to be a phenomenon of heredity and segregation. Experimental evidence of its validity was furnished as early as 1907 by Correns, who studied hybrids between monoecious and dioecious species of Bryonia. His results indicated that in the dioecious species sex was determined by the pollen grain of which there were two kinds equal in number, one being male-producing and the other female-producing whilst the ovules were all of a kind. Correns compared the combinations resulting from the union of the two forms of pollen grain with the one form of ovule with those of the typical back-cross of a Mendelian experiment in which the heterozygous dominant (Dd) mated to a recessive (dd) yields equal numbers of heterozygous dominants and recessives.

	Dd	×		dd	
D		d	:	d	gametes
Dd		:		dd	

Doncaster (1906), working with the currant moth *Abraxas grossulariata*, produced evidence that strongly suggested

that in animals also sex-determination was due to segregation of hereditary factors.

Bateson and Punnett (1908), basing their interpretation on the assumption that the character femaleness was dominant to the contrasted character maleness, and that the female in Abraxas was always heterozygous in respect of the character femaleness, devised a scheme, of considerable historical interest, to show the relationship of the sex of the individual to its colour pattern. If the hereditary factor for the grossulariata colour pattern is symbolized by G, that for lactocolor by g, that for the dominant femaleness character by F, and that for the recessive maleness character by f, then the results of Doncaster's experiments can easily be accommodated, if it is assumed that the female is always constitutionally heterozygous (Ff) for the character femaleness, and further, that the two dominant factors G and F repel each other so that they can never be present together in the same gamete.

The results of the breeding experiments carried out by Doncaster were as follows:

1. lacticolor ♀ × gross. ♂=gross. sons and daughters. Gross. was dominant to lacticolor.
   In the F.2 both gross. and lact. occurred, there being on the average in every 4, 3 gross. to 1 lact. Among the gross. individuals there were both males and females but the lacticolors were all females.
2. F.1 gross. ♂ × lact. ♀=gross. and lact. individuals in equal numbers and among both of these types males and females in equal numbers.
3. lact. ♂ from 2 × F.1 gross. ♀=equal numbers of gross. and lact. individuals but all the gross. were males and all the lact. were females.
4. lact. ♂ from 2 × wild gross. ♀=equal numbers of gross. and lact. individuals but all gross. were males and all lact, were females.

Bateson and Punnett's explanation of these results was as follows:

1.	lact. ♀	×	gross. ♂	
	ggFf		GGff	P.1
	gF gf	:	Gf	gametes
	GgFf		Ggff	F.1
	gross. ♀		gross. ♂	

Gf gF (repulsion) : Gf gf gametes
GGff Ggff GgFf ggFf F.2
gross. ♂ gross. ♂ gross. ♀ lact. ♀

2. lact. ♀ × F.1 gross. ♂
ggFf Ggff
gF gf : Gf gf gametes
GgFf ggFf Ggff ggff
gross. ♀ lact. ♀ gross. ♂ lact. ♀

3. F.1 gross. ♀ × lact. ♂
GgFf ggff
Gf gF (repulsion) : gf gametes
Ggff ggFf
gross. ♂ lact. ♀

4. wild gross. ♀ × lact. ♂
GgFf ggff
Gf gF (repulsion) : gf gametes
Ggff ggFf
gross. ♂ lact. ♀

Since the time when this explanation of what is now known to be an instance of the inheritance of sex-linked characters was offered, the sciences of cytology and genetics have expanded vastly and out of their development emerged the current theory of sex-determination. By this theory all the older hypotheses of sex-determination have been rendered obsolete and, save for historical purposes, can be disregarded. The framework of this theory consists of secure knowledge concerning the constant and significant differences between male and female in respect of their sex-chromosome and therefore of their genic constitution and, secondly, concerning the observed facts relating to the phenomenon of sex-linkage, which enables the observer to trace the transmission of sex-chromosomes from generation to generation. The primary difference between the sexes is now known to be a chromosomal and a genic difference. In the bisexual and dioecious species the sex of the individual, as a general rule, is now known to be decided at the moment of fertilization by the interplay of the sex-chromosome constitutions of the uniting gametes. This chromosomal,

genetic, theory was confirmed by the correlation that has been observed between the distribution in inheritance of the sex-chromosomes and of the sex-linked characters. Nothing that has been encountered during the last fifty years has required any significant modification of this theory. At present it seems distinctly unlikely that this theory will be at all seriously shaken in foreseeable time, but new discovery in other scientific fields may, in its impact upon biological science, necessitate its review and revision.

CHAPTER 2

THE SEX-CHROMOSOMES AND SEX-DETERMINATION

In a very large number and in a wide variety of species it has been shown that the male is to be distinguished from the female by constant differences in the chromosome content of the nuclei of their component cells. This difference takes several forms. In certain species one sex possesses one chromosome less than does the other, that is to say in one sex the chromosomes are all paired whilst in the other one member of one pair is lacking. In other species both sexes possess the same number of chromosomes, existing in pairs, but in one sex one particular pair consists of chromosomes unequal in size and shape.

The single unpaired chromosome found in one sex and the pair in the other to which it corresponds, and the pair of chromosomes in respect of which the sexes differ, are known as the sex-chromosomes in order to distinguish them from the rest of the chromosomes in respect of which both male and female are alike. These are known as the autosomes. The single chromosome found in one sex and the pair in the other to which it corresponds and, in the case of the species in which the chromosome number is the same in both sexes, that chromosome which is found in both male and female, are known as X-chromosomes. The unequal mate of the X in one of the sexes is known as the Y-chromosome. Thus in respect of sex-chromosome constitution the sexes can be described as:

XO:XX
or XY:XX

The third form which this difference between the sexes takes is that in which the sex-chromosomes are represented not by single elements but by groups which during gameto-genesis behave as one compound chromosome. Whatever

the number of X-chromosomes within the group, the group itself is single in one sex, double in the other, so that essentially this difference is of the XO:XX type or, as is sometimes the case, XY:XX, for the single compound X is in certain species associated with a Y-chromosome. Ray-Chaudhuri and Manna (1950) report that the male of the gryllid Euscyrtus is X^1X^2Y. The Y can itself be compound. Thus in the dioecious plant *Rumex acetosa* Kihara and Ono (1923) found a Y-chromosome consisting of two elements in association with a single X. According to Sharman, McIntosh and Barber (1950) the rat kangaroo is XY^1Y^2 in the male, XX in the female.

The first account of a sex-chromosome difference was that of Henking (1891), who described in the bug *Pyrrhocoris apterus* a peculiar chromatin element which was condensed in the early prophase of the primary spermatocyte. In the first spermatocyte division the twelve elements found in the metaphase plate all divided equally, but in the second division one of the twelve elements lagged and finally passed undivided into one of the two daughter cells. As a result two kinds of spermatids were formed, one with eleven and one with twelve of these elements. Henking did not at this time refer to this odd chromatin element as a chromosome but called it a 'nucleolus'. He did not confuse it with a true nucleolus, however.

In 1898 Paulmier recorded a similar phenomenon in *Anasa tristis*, in the second spermatocyte division of which eleven chromosomes passed to one pole and ten to the other. In 1901 de Sinety described the behaviour of what he called a 'chromosome spécial' in the male of Orphania. In the same year McClung suggested that the two classes of spermatozoa resulting from the meiotic distribution of the 'accessory' chromosome must be causally related to the production of the two sexes. 'Upon the assumption that there is a qualitative difference between the various chromosomes of the nucleus it would necessarily follow that there are formed two kinds of spermatozoa which, by fertilization of the egg, would produce individuals qualitatively different. Since the number of each of these varieties of spermatozoa

is the same, it would happen that there would be an approximately equal number of these two kinds of offspring. We know that the only quality which separates the members of the species into these two groups is that of sex.'

Thus it was that the chromosome complex came to be associated with sex-determination. McClung's main hypothesis was complicated by its association with a subsidiary one of selective fertilization which led him to the conclusion that the spermatozoon carrying the extra chromosome was male-determining. If this were so, then the male had to be the sex which had one chromosome more than did the female. Sutton (1902), by reporting that the spermatogonia of Brachystola possessed one chromosome more than did the ovarian follicle cells, provided support for McClung's error.

The work of McClung aroused great interest and much controversy. It evoked great activity in the field of cytology. Gross (1906) claimed to have demonstrated that in Syromastes and Pyrrhocoris the accessory chromosome (the single, unpaired one) present in the spermatocytes arose from two small spermatogonial chromosomes and, further, that the number of chromosomes was the same for both sexes. It was his opinion that all spermatozoa lacking the accessory chromosome degenerated so that only one type of functional gamete remained. However, Stevens (1905) in the beetle Tenebrio and Wilson (1905) in the bug *Lygaeus furcicus* showed clearly that in these forms at least there was one pair of unequal chromosomes and that this pair behaved in the growth stages of the spermatocytes exactly like the unpaired accessory chromosome. They found also that the members of this unequal pair separated and passed to opposite poles in one of the two meiotic divisions. Stevens further demonstrated that the diploid number of chromosomes was the same in both sexes but that in the female no pair consisting of unequal mates was present, the male being XY, the female XX. Then in 1909 Wilson corrected Gross by showing that in the male of Pyrrhocoris there was an unpaired chromosome in the spermatocyte and that this arose from a single spermatogonial chromosome of corresponding