thyreoidea im Winterschlaf vermutet[86], und auf Grund von licht- und elektronenmikroskopischen Befunden an Hamstern schliesst Kayser[87,88] auf eine – vor allem jahreszeitlich bedingte – erhöhte Tätigkeit dieser Drüse im Winterschlaf. Dazu würde nicht nur der Anstieg des Calciums im Serum, sondern auch sein Abfall im Skelett des Igels passen; auch die Erhöhung des Serum-Magnesiums könnte teilweise dadurch bedingt sein[89]. Beweisend wäre eine entgegengesetzte Verschiebungstendenz des anorganischen Phosphats im Blut, da die Nebenschilddrüse für seine Regulation gleichfalls ausschlaggebend ist. Aus neueren Zusammenstellungen über den Phosphorhaushalt der Winterschläfer[90,91] ist zu entnehmen, dass das anorganische Phosphat beim Igel, Goldhamster und Ziesel im Winterschlaf ansteigt und nur beim Steppenmurmeltier etwas abnimmt[14]. Die Phosphaterhöhung dürfte jedoch mit dem Kohlenhydrathaushalt, besonders der fehlenden Zuckerverwertung infolge Insulinmangels im tiefen Winterschlaf zusammenhängen[91].

Magnesium ist, wie Kalium, gegenüber dem Blutplasma intrazellulär angereichert. Die Ähnlichkeit besteht auch in der gleichermassen vorhandenen Beziehung zum Kohlenhydrathaushalt: Insulin und Traubenzucker fördern beim Kaninchen die Magnesiumaufnahme in die Knochen und die Zellen aller Organsysteme[92]. Die bisherigen Ergebnisse (Tabelle VI) lassen aber nicht erkennen, ob diese Parallelität zwischen Kalium und Magnesium auch für den Winterschlaf zutrifft.

Eine endgültige Klärung der Zusammenhänge zwischen Mineralhaushalt und dem endokrinen System wird erst bei gewissenhafter Berücksichtigung der Körpertemperatur im Winterschlaf möglich sein. In den meisten Fällen scheinen die Veränderungen dieses Zusammenspiels nicht die Ursache, sondern die Folge des Winterschlafs zu sein.

Summary. A review is presented on the metabolism of sodium, potassium, calcium and magnesium during natural hibernation in mammals, and its relation to endocrine activity. With the entrance into hibernation, a change of homeostasis and an initial vago-insular stage occur, resulting for instance in a hyperpotassemia. When the body temperature falls further, a sympathicoadrenal stage is observed whilst the serum potassium attains its normal level, probably favoured by simultaneous activation of the zona glomerulosa. Most animals show an increase of serum calcium and magnesium in hibernation in consequence of anhydremia, as well as of probably parathyreoid activity. It is suggested that an aldosterone and/or ADH secretion is provoked by diminishing of the intravasal space in deep hibernation. The mineral metabolism of bats differs in several points from that of other hibernators.

[86] St. Skowron und St. Zajaczek, C.R. Soc. Biol. Paris *141*, 1105 (1947).

[87] Ch. Kayser, A. Petrovic und A. Porte, C.R. Soc. Biol. Paris *155*, 2178 (1961).

[88] A. Porte, Ch. Kayser, A. Petrovic und M. E. Stoeckel, C.R. Soc. Biol. Paris *157*, 370 (1963).

[89] P. L. Munson, Ph. F. Hirsch und A. H. Tashjian jr., Ann. Rev. Physiol. *25*, 325 (1963).

[90] M. A. Brock, Amer. J. Physiol. *199*, 195 (1960).

[91] R. Kristoffersson, Annal. Acad. Sci. Fenn. Ser. A IV Biologica *50*, 1 (1961).

[92] J. K. Aikawa, Proc. Soc. exp. Biol. Med. *103*, 363 (1960).

Polygenic Sex Determination*

By Curt Kosswig**

Zoologisches Staatsinstitut und Zoologisches Museum Hamburg (Germany)

All organisms which reproduce bisexually have a bisexual potency, even in such cases in which the production of male and female germ-cells occurs in different individuals, males and females respectively. In primitive forms there are indications that this bisexual potency is even present in the sexually differentiated gametes themselves; the well-known phenomenon of relative sexuality may be mentioned in this connection. It is a characteristic of this generally present bisexual potency that its manifestation in the phenotype is a distinctly alternative one. Even in typical hermaphrodites, each single cell is able to manifest either the male or the female component of this potency, the two never being activated at once in the same cell. This is true not only for the primary sexual characters, the gonads and their gametes, but also for the secondary sexual characters in morphology, physiology and behaviour, so abundantly represented in higher animals. (An exception must be made for characters

---

* Lecture given at the University of Baghdad (April, 1962).

** With the aid of the Deutsche Forschungsgemeinschaft.

evoked by genes in the Y-chromosome.) It is true that we have no exact knowledge about the localization of the determining factors of this bisexuality with an alternative manifestation in the phenotype. Possibly a very great number of Mendelian genes in all chromosomes of the haploid set form the material basis of this bisexuality which, in diplobiontic animals, manifests itself in the haploid (gametic) and in the diploid (zygotic) stage. If this is the case, we have to imagine that even small regions of one chromosome bear an interbalanced set of genes assuring maleness and femaleness. Otherwise the continuation of the hermaphroditic state in monoecious plants with a hyperploid chromosome set (e.g. in *Datura*) could not be understood (BLAKESLEE[1]. On the other hand, we have to keep in mind that the representation of the bisexual potency in the formula of HARTMANN[2] (AAGG for the zygotic, AG for the gametic phase) is an absolutely formal one, not proved by any localization experiments. HARTMANN's A's and G's are supposed to be present in a homozygous state, thus an analysis of their loci is impossible. But we cannot exclude the other possibility that the determining factors of bisexuality may be localized outside the chromosomes, somewhere else in the hereditary material. Not to anticipate results of later research, it seems sounder either to renounce any representation in our genetic formula or to show by Σ our practically complete lack of knowledge about the localization of the bisexual potency in the idiotype.

The realization of the male or the female ability in the phenotype depends either exclusively on conditions of the outside and/or inside environment, within which the development of an individual of a given species occurs (as in all different types of hermaphrodites), or also on Mendelian genes (the realizators or sex-genes s. str.). By these sex-genes, one side of the bisexual potency is activated while the other is suppressed, and *vice versa* (CORRENS[3]). In the latter case of sex-realization with participation of Mendelian genes, generally gonochoristic individuals are formed, that is producers of only one type of germ-cell, either spermatozoa or ova in multicellular animals. As we shall see later, even in such well-known organisms as *Drosophila*, our exact knowledge about the number and the localization of the sex-genes is poor; but certainly the number of different ways by which sex is realized by the action of Mendelian genes is much greater than, for example, HARTMANN[2] tried to tell us.

It is a well-known fact that in many gonochoristic species in the *Metazoa* the primary sex ratio in each generation is 1:1. In organisms with sex realization in the diploid phase, this corresponds to the results of the back-cross of a monohybrid (Aa) with either of its homozygous parent forms (AA or aa). According to this principle, one of the two sexes, the heterogametic one, produces male and female determining gametes in equal number, while the other, the homogametic one, produces only one type of gametes. As MULLER[4] put forward many years ago, the sex-realization-mechanism can be imagined formally as being based upon a single sex-deciding gene and its allel. MULLER[4] compared the situation with a solution of an indicator substance to which a drop of acid is added. No change in colour occurs as a result of sufficient buffering in the solution. But addition of a further drop of acid will alter the situation and the colour of the solution will change. When we consider the fact that all important characteristics of an animal – and sex certainly is an important characteristic – have a polygenic basis, it becomes very doubtful, at least for a prolonged evolution upon a gonochoristic line, that sex should still depend on only one pair of allels. Even in corn, a typical hermaphrodite, mutations at two loci have to be combined for the production of male-sterile, i.e. female, plants and *vice versa* (JONES[5]).

In earlier years, it seemed to be a riddle that large systematic units, e.g. orders, showed the same situation as far as the sex-determining principle was concerned. All mammals seem to have heterogametic males, whereas in birds the female is the heterogametic sex. This might be the result of descent from a common ancestor of all modern birds. In the teleostean fishes, on the other hand, a group in which evolutionary changes are going on on a large scale, even different populations of the same species are heterogametic in either the male or the female sex (GORDON[6], KOSSWIG[7]).

The discovery of sex chromosomes in many organisms was a strong argument in favour of the monohybrid back-cross principle in sex determination: the homogametic sex having two equal X-chromosomes, the heterogametic being XY. Very soon, however, cases became known in which the heterogametic sex had only one X-chromosome, a Y not being present at all. In such examples, one of the two sexes, namely the heterogametic one, has no allel of the sex-deciding gene mechanism. In the case of male heterogamety, as in *Protenor*, the question arises where the genes for the heterogametic (male) sex are localized. Here the quantitative explanation given by GOLDSCHMIDT[8] was very useful and could be proved to be correct in many cases. In species with XO-males, according to this author, the male-determining genes are localized in the autosomes which are equal in the two sexes, whereas the

[1] A. F. BLAKESLEE, Z. ind. Abst.-Vererb.-lehre Suppl. Bd. *1*, 117 (1928).

[2] M. HARTMANN, *Die Sexualität* (Gustav Fischer Verlag, Stuttgart 1956).

[3] C. CORRENS, Handb. Vererbungswiss. *2*, C, *1* (1928).

[4] H. J. MULLER, Amer. Nat. *64*, 118 (1932).

[5] D. F. JONES, Genetics *19*, 552 (1934).

[6] M. GORDON, J. Hered. *37*, 307 (1946).

[7] C. KOSSWIG, Züchter *7*, 40 (1935).

[8] R. GOLDSCHMIDT, Bibliogr. Genet. *11*, 1 (1934).

female-determining genes were supposed to be localized in the X's. Accordingly, the formula for the homozygous *Protenor*-♀ is $X_FX_FA_MA_M$ and for the male $X_FOA_MA_M$. 2F being much stronger than 2M, and the latter stronger than 1F, the principle of sex realization in a formal scheme can be based upon 2 gene pairs. One of them would be present in a homozygous form in the two sexes (and would therefore not be proved to exist by direct methods), the other would be present twice in the one and once in the other sex. But again, as in HARTMANN's formula for the bisexual potency, we are confronted with the fact that a localization analysis of the F- and M-genes, and consequently a decision between the number of pairs of actually participating genes, is practically impossible. Nevertheless, the heuristic value of GOLDSCHMIDT's hypothesis cannot be underestimated. It is important to note that later experiments with *Drosophila* demonstrated that, for this genus too, GOLDSCHMIDT's formula can be applied: The Y of *Drosophila* bears no sex-deciding genes – and this is the reason why the Y-chromosome plays a male-determining role under normal conditions.

Through the discovery of the so-called triploid intersexes in *Drosophila melanogaster*, GOLDSCHMIDT's theory received a most remarkable experimental proof. Real triploids (3X 3A) are typical females; the combination 2X 3A, on the other hand, results in intersexes, i.e. individuals which up to a certain time-limit develop in the female direction; after which, development turns to the contrary male differentiation so that intersexes are sexual mosaics in time. The appearance of intersexes is readily understood by assuming that the 2F in the X's are approximately equal in their effect to the 3 series of M-genes in the 3 sets of autosomes. As shown by BRIDGES[9] and by DOBZHANSKY and SCHULTZ[10], it is possible to select lines in which the degree of intersexuality can differentiate either towards the male or the female phenotype. This seems to indicate that the M in our formula is only the representation of many genes all acting together towards maleness. The fact that some of these genes are present in the stage of at least two allels makes possible the positive result of selection experiments. Only as a result of the delicate balance in the 2X3A-individuals, can the effect of selection of minor individual M-allels be observed. For this reason, later criticisms by GOLDSCHMIDT[11,12], rejecting the idea of a polymeric system of male-determining genes all over the autosomes, do not seem satisfactorily based.

A further, even more convincing proof for the existence of a system of multiple sex-genes, now in the X-chromosome, was obtained using again the triploid intersexes (2X3A). Two combinations of this type, fragments of the euchromatic region of an additional part of an X were added. By this method two comparable types of intersexes in the same brood were obtained: the one of the normal constitution 2X 3A and of a certain degree of intersexuality phenotypically, and the other with an additional fragment $2\,X\,X_{fr}\,3\,A$. Using different parts of the X of different lenghts, it could be proved in a great number of diverse experiments (DOBZHANSKY and SCHULTZ[13]) that each addition of such a fragment, corresponding to its length, caused a shift towards femaleness in the individuals in question. This is why we have to conclude that each part of the euchromatic region of the X is the carrier of genes acting towards femaleness. GOLDSCHMIDT's formula X_F was oversimplified. In reality it is simply the expression of a great number of polymeric genes in the X acting in the female direction. While some hundred loci in the euchromatic region of the X were exactly located, this could be done for none of the F-genes. This means that the number must be so high, and their specific degree of action of each of them so low, that the idea of definite loci of F-genes in the X of *Drosophila* is practically substituted by that of an indefinite number of polygenes, the effectiveness of which is measurable only with the length of the X-fragment involved. In so far as a polygenic concept of sex-determination is applicable also to *Drosophila*, the speciality of which is – in accordance perhaps with many other organisms with the XO(Y)-type of sex-determination – the type of distribution of the majority of sex-genes in the mode emphasized by GOLDSCHMIDT.

In chironomids it was found that a certain segment attached to a given chromosome is the carrier of male-determining genes (BEERMANN[14]). This segment can be attached either to one or the other of the haploid set of chromosomes of these forms. The chromosome which bears the segment in question becomes the Y-chromosome. Only one male-determining section can be present in order to assure the development of a male. Therefore, even in the same population, one type of female $X_1X_1X_2X_2AA$, but two types of males, $X_1Y_1X_2X_2AA$ or $X_1X_1X_2Y_2AA$, are possible. There are good reasons to believe that the M-genes in these forms are localized in the transportable section, whereas we have no knowledge about the localization of female-determining genes in this case. F-genes may be situated in the X's, in the autosomes, or in both; a decision between these possibilities is difficult. Nevertheless it seems to be true that, in the case of *Chironomus*, a single dose of M-genes in a transferable chromosomal segment is stronger in its phenotypical effect than the sum of F-genes in the double set of autosomes and/or X's. A somewhat similar situation was observed in some Cyprinodontid fishes, e.g. in *Lebistes*

---

[9] C. B. BRIDGES, Amer. Nat. *56*, 51 (1922).

[10] T. DOBZHANSKY and J. SCHULTZ, Proc. Nat. Acad. Sci. *17*, 513 (1931).

[11] R. GOLDSCHMIDT, Proc. Nat. Acad. Sci. *34*, 245 (1948).

[12] R. GOLDSCHMIDT, Arch. Julius Klaus-Stiftung *23*, 539 (1948).

[13] T. DOBZHANSKY and J. SCHULTZ, J. Genet. *28*, 349 (1934).

[14] W. BEERMANN, Biol. Zbl. *74*, 525 (1955).

(Winge[15,16]) and in *Platypoecilus* (Gordon[6,17]). It is highly probable that a segment of the Y, non-homologous to any section of the X, bears the realizator for the heterogametic sex[18]. In *Lebistes* this is normally the male; in *Platypoecilus maculatus* it is either the male or the female depending on the geographic position of the population. In the case of male heterogamety, it could be proved for *Platypoecilus* that the X-chromosomes bear female determiners, the M-gene (or a complex of them) being localized in a specialized segment of the Y. But in the autosomes, too, there are genes contributing to sex-determination. Öktay[19,20] was able to show that in an incest-line of *Platypoecilus maculatus* from Mexico, males of the constitution XX occurred. Until now, Öktay has succeeded in producing such exceptional XX-males by brother-sister matings during 9 generations (Figure 1). The hereditary basis of this type of male production is beyond any doubt. Outcrossing of XX-exceptional males to normal XX-females results practically only in female progeny. On the other hand, interbreeding of males and females of the exceptional line led to both sexes in extremely variable proportions in different crossings.

The situation in Öktay's exceptional line finds a satisfying interpretation on the following basis. The presence of at least a certain number of M-genes, localized in different autosomes, has to be assured by a recombination effect during meiosis and zygote formation. Only those individuals which bear so many M-genes that the threshold for male differentiation is reached become males. Other combinations without M-genes (if there are any) or with a number below the threshold value will differentiate into females. Naturally it is also possible, and to be expected, that such males will be produced which bear more M-genes than necessary for reaching the threshold. The latter may be called strong males. The strength of a male cannot be recognized in its phenotype. All males reach sexual maturity approximately at the same age and at the same body-length. Strong and weak males can be distinguished from one another only by the number of male offspring they produce with a given female. The strong male will have a higher percentage of male offspring than a weak one. In practice such an experiment is not easily performed because *Platypoecilus* is a viviparous fish, one copulation being sufficient for a number of broods. As will be mentioned later, the correctness of this view could be proved using (Breider[21]) 'marked' spermatozoa (bearing dominant colour genes) in *Xiphophorus helleri*, which in general has this type of polygenic sex-determination resulting from a more or less high number of freely combinable genes localized in its 'autosomes' (Table I and II). This is why, in extending the exceptional line of her XX-Platys, Öktay is obliged to work somewhat 'in the dark', as neither the strength of the male used in a certain cross is known nor the number of M-genes below the threshold-line is to be recognized from the phenotype of a female. A weak female will produce a higher percentage of males than a strong one, when the two are coupled with the same male, whatever the strength of the latter may be. This experiment has been performed many times by Öktay and also earlier with other forms by other authors (Kosswig[22], Breider[23], Rust[24], Schwier[25], Aida[26]).

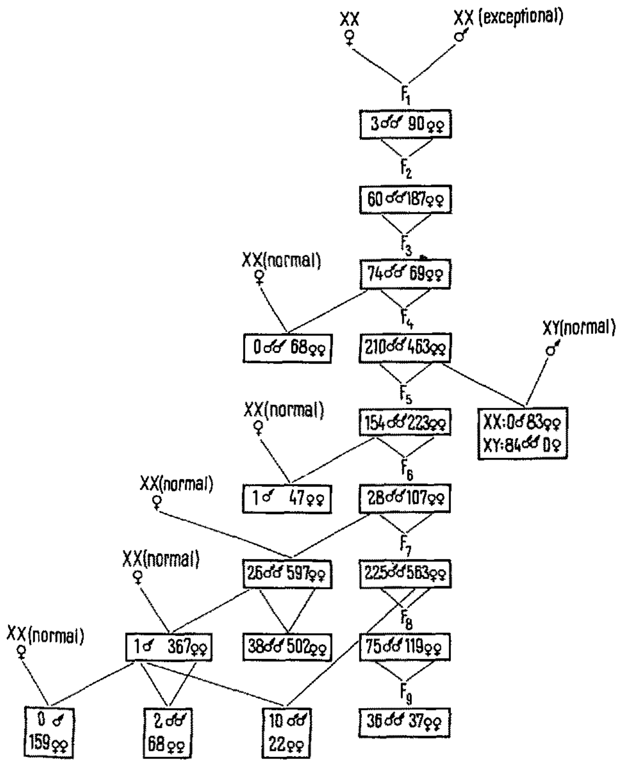

Fig. 1. Schematic representation of Öktay's experiments with a *Platypoecilus maculatus* form showing polygenic sex determination. Outcrossing with the normal stock results practically in the restitution of the monogenic sex determination type.

---

[15] Ö. Winge, C. R. Labor. Carlsberg Ser. phys. *21*, 1 (1934).

[16] Ö. Winge and E. Ditlevsen, C. R. Labor. Carlsberg Ser. phys. *24*, 227 (1948).

[17] M. Gordon, Zoologica *36*, 127 (1951).

[18] Here it may be added that in the mammals principally the same type of localization of sex-deciding genes is present as in *Chironomus* or in the Cyprinodontid fishes. In the male sex all mammals bear a Y-chromosome. In the Y-chromosome – according to our present knowledge – the male determining gene (or genes) is localized. On the other hand the XO-type, which in *Drosophila* results in the production of males, yields females which at least in the mouse are completely normal and fertile. In man the same situation is principally true too.

[19] M. Öktay, Istanb. Üniv. Fen Fak. Mecm. B *24*, 75 (1959).

[20] M. Öktay, Istanb. Üniv. Fen Fak. Mecm. B *24*, 225 (1959).

[21] H. Breider, Zool. Anz. *106*, 277 (1934).

[22] C. Kosswig, Z. ind. Abst.-Vererb.-lehre *57*, 226 (1931).

[23] H. Breider, Z. ind. Abst.-Vererb.-lehre *68*, 265 (1935).

[24] W. Rust, Z. ind. Abst.-Vererb.-lehre *79*, 336 (1941).

[25] H. Schwier, Z. ind. Abst.-Vererb.-lehre *77*, 291 (1939).

[26] T. Aida, Genetics *21*, 136 (1936).

Table I. *X. helleri*, progenies of different females, all paired with the same male (after BREIDER[27])

♀♀	Number	Number of offspring		% of ♂♂
		♂♂	♀♀	
Fr.	1	71	297	19.3
	2	146	449	24.5
	3	121	230	34.5
	4	40	259	13.4
	5	56	90	38.4
	6	223	305	42.2
Cr.	9	337	155	68.5
	17	167	52	76.3
	19	161	62	72.2
	25	52	36	59.1
	29	42	35	54.6
Z. 200 N	7	116	57	67.1
	8	171	24	87.7
	10	179	84	68.1
	15	55	41	57.3

Table II. *X. helleri*, two females paired with different males, distinguishable from one another by the presence or absence of a dominant colour gene. The females were heterozygous for the dominant colour gene Mo (after BREIDER[27])

♀	Phaenotype of progeny	Sex ratio (in %) in the progeny of			
		♂ 1		♂ 2	
		♂♂	♀♀	♂♂	♀♀
Momo$_1$	Momo	5.7	94.5	37.5	62.7
	momo	43.8	56.2	62.5	37.5
Momo$_2$	Momo	7.6	92.4	27.9	72.1
	momo	62.9	37.1	70.0	30.0

Another factor by which the predictability of the sex-ratio of the offspring and the evaluation of the sexual strength of the parents becomes complicated and problematic is the following: The genic system in cases of so-called polygenic sex determination is based upon a series of pairs of allels; each allel works together with its partner in the homologous chromosome and with all others localized in other chromosomes. This means that sex-determination is assured by a system of polygenes with an additive polymeric action of each of its members. Let us suppose that at least three genes of this polymeric system are necessary to produce a male. The number of loci of participating pairs of allels may be as small as four (A/a, B/b, C/c, D/d). Then the following combinations with only 3 genes of the participating loci will result in the production of males:

1. Aa Bb Cc dd
2. Aa Bb cc Dd
3. Aa bb Cc Dd
4. aa Bb Cc Dd
5. AA Bb cc dd
6. AA bb Cc dd
7. AA bb cc Dd
8. aa BB Cc dd
9. aa BB cc Dd
10. aa bb CC Dd
11. aa bb Cc DD
12. Aa BB cc dd
13. Aa bb CC dd
14. Aa bb cc DD
15. aa Bb CC dd
16. aa Bb cc DD

Let us use 2 males (no. 1 and 5 of the combination scheme) and cross them with a strong female not having a single one of the male-determining genes A, B, C or D; being aa bb cc dd. Only one type of egg is produced by such a female: ab cd (d being also present in the homozygous condition in the 2 males it can be neglected). By the male no. 5 (AA Bb cc) two types of spermatozoa are produced: ABc and Abc. Their combination with abc-eggs will result in two types of zygotes, 50% having two, the other 50% having only one male-determining gene. Therefore the whole brood will consist of females (of medium and of weak strength respectively). The other male, no. 1, with the constitution Aa Bb Cc will produce 8 types of spermatozoa, only one of them bearing 3 genes for maleness. The sex-ratio of this male with the same female (aa bb cc) will be 1♂:7♀. In the case where we combine the same male (Aa Bb Cc) with a weak female (Aa Bb cc), the progeny would consist of males and females in equal number. Resuming, we can say that there is an enormous degree of relativity in the sex determination process on the basis of polymeric genes, because the sexual strength of an individual is dependent (1) on the number of sex-genes it bears, and (2) on the degree of heterozygoty for the participating genes. By the two conditions mentioned, the sexual strength of the different progeny is also influenced. In cases of polymeric sex-determination, any prediction of the sex ratio in a certain cross is highly doubtful. The only way to prove the correctness in principle of the interpretation lies in the possibility of producing lines rich in males and others rich in females by selection continued over many generations. Selection will be easier when the number of participating pairs of allels is relatively small.

In our interpretation given above, the polymeric system of genes was assumed to be exclusively built by genes, each of which had exactly the same quantitative effect. This assumption lacks proof. It is well possible that our polygenic system consists of members of different effectiveness, i. e. 'major' genes and 'minor' genes. A further complication may also be encountered. We do not really know whether the loci involved are present in only two allelic stages. Cases in which, at a given locus, multiple allels may occur even inside one gene pool, cannot be excluded. We therefore have to admit that the interpretation given here for polygenic sex-determination on the basis of an additive polymery is a highly formal one. But are we not confronted with more or less the same situation in the classical examples

---

[27] H. BREIDER, Z. wiss. Zool. (A) *146*, 383 (1935).

of sex-determination too? Also in *Drosophila* so many genes participate in sex-determination that their number and their loci could never be exactly indicated; and *Drosophila* is the best-known object in animal genetics. Cases like the male-determining segment in *Chironomus*, and perhaps in *Lebistes* and some *Platypoecili*, or the euchromatic region of the X-chromosome evoking femaleness in *Drosophila*, are outstanding examples for a deeper analysis of sex-determining genes (the exact localization of a series of multiple allels controlling sex in *Habrobracon* (WHITING[28]) is an item outside this discussion when we consider the fact that the determination of sex in *Hymenoptera* normally depends on the haploidy or diploidy of the individual). Although the participation of many genes in sex-realization is proved, or very probable, in animals with the normal XX- or XY-mechanism, the balance between F- and M-genes is regulated by their quantitative and/or their epistatic behaviour depending on their localization. In these forms, perhaps as a result of a long and adaptive evolution, each of the two systems is built up by a great number of minor genes, each of which is able to mutate only to an allel also of minor activity. In both systems +- and −-mutations may occur which, counterbalancing among each other under normal conditions, never reach the level at which the mechanism as a whole would be affected or broken down. In cases of ordinary polygenic (polymeric) sex-determination, the abolition of its mechanism is more easily effected because the balance between inherited male and female tendencies can be overcome by relatively few mutations.

It was mentioned above that the formulae by which polymeric sex determination is described are formal and relative. As examples for one of ÖKTAY's *Platypoecili*, 3 capital letters A, B, and C were chosen to represent male-determining genes. It is practically impossible to decide whether A, B, and C are actually M-genes in a strict sense, or whether they are 'losses' of genes acting towards femaleness. In the first case, the question arises: if A etc. are loci acting positively towards maleness by their structure, how do the allels a, b, c etc. act then? Are they neutral in the sex-realization process or do they act specifically towards femaleness? No exact answer can be given to this question. But we can imagine that in organisms with polymeric sex-realization there are two systems of polygenes: the one working towards maleness, the other towards femaleness, each of them being either completely or partially independent of the other in their inheritance, or being completely interdependent due to the fact that one allel of each pair works as a male-determining and the other as a female-determining gene. In general, the mode of description of the situation used above, i.e. representation by one polymeric system acting in one sexual direction while the tendency for the other sex is accepted as being constant (homozygous), seems to cover all the known facts.

The work of ÖKTAY was used above as a good example to demonstrate polygenic sex-determination on a polymeric basis. Yet the first results which supported this hypothesis were obtained 30 years before ÖKTAY's experiments were carried out. Since then a number of fish species in the genera *Xiphophorus*, *Limia*, *Macropodus* were found to be polygenic in their sex determination not as a result of domestication but of nature. A private communication of the late Dr. M. GORDON may be of interest in this connection. In a population of *Platypoecilus maculatus* from Lake Peten in Yukatan, certain colour-genes which are transferred in the X- or Y-chromosomes of the Mexican population, and in the Z's or W's of that from British Honduras, do not show sex-linked inheritance. This fact is in favour of the assumption that a situation similar to that of ÖKTAY's material also exists in nature. The most famous representative for polygenic sex-determination s. str. is the swordtail, *Xiphophorus helleri*. As early as 1933, KOSSWIG[29], BREIDER and KOSSWIG[30], and BREIDER[27] were able to report on experiments with thousands of fishes; the contradictory results obtained, found an easy interpretation through KOSSWIG's[31] assumption that there are no sexually different gonosomes, i.e. X's and Y's, in *X. helleri*, but that merely polygenes and their manifold recombinations decide about the sex of a specimen. Experiments with *X. helleri* are still going on in our laboratory and no essential corrections in the original theory have become necessary. Whereas in lines of *X. helleri* used in earlier research, and under given laboratory conditions, it was not possible to distinguish between strong and weak males, my student PETERS found that in *X. helleri guentheri* from Honduras two types of males can be distinguished; besides the 'normal' type of males there is a second type, called late males, which become larger and differentiate sexually more slowly than the normal ones. Crossing a normal and a late male with the same female generally results in more males in the progeny of the 'normal' male, which would be the stronger one. That there is a certain correlation between strength of male and time of sexual differentiation in *Xiphophorus* became probable very early (KOSSWIG[22]). In F_2-generations of *X. helleri* and *Platypoecilus maculatus*, a type of grey male is frequent besides some grey females. They bear the sex-indifferent chromosomes of *X. helleri*, which are homologous to the gonosomes of *Platypoecilus*, marked with dominant colour genes. In most cases these grey males are dwarfs completing their

---

[28] P. W. WHITING, Genetics *28*, 365 (1943).

[29] C. KOSSWIG, Roux' Arch. Entw.-mech. *128*, 393 (1933).

[30] H. BREIDER and C. KOSSWIG, Verhdlg. Dtsch. Zool. Ges. *1937*, 275.

[31] C. KOSSWIG, Roux' Arch. Entw.-mech. *133*, 140 (1935).

sexual differentiation in 6–10 weeks after birth. With the start of male maturity, growth is not stopped but remarkably reduced. The frequency of these dwarf males and their rapid sexual differentiation may also have its reason in their polygenic determination. As a result of the species' cross in the F_2-recombinations, there may occur accumulation of M-genes of the two grandparent species and/or elimination of female determiners of *Xiphophorus*. If this interpretation is correct, dwarf males crossed with *X. helleri*-females must manifest themselves as very strong males with a high percentage of male progeny. Unfortunately dwarf males are of such a small size that they cannot copulate easily with the much larger *helleri* females. But by artificial insemination the strength of such a dwarf male can be measured, especially when the female is inseminated at the same time by marked spermatozoa of a normal or a late male. The result is clear and convincing: dwarf males produce more male progeny than the other males (Table III).

In fish it is possible to cross different species with one another, even if one of them has the polygenic and the other the 'monogenic' type of sex-determination. The theory of polygenic sex-determination was founded on such species crosses. It is interesting to note that in these crosses, depending on the species used, either the polygenic or the monogenic type can be the epistatic one. Thus, for instance, in the F_1 between a *X. helleri* ♀ and a *P. maculatus* ♂ (ZZ or XY), the two sexes appear in each combination, i.e. males and females occur in the Zx-, Xx- and in the Yx-classes (x represents the 'autosome' of *X. helleri* which is homologous to each of the gonosomes of *Platypoecilus*). On the other hand (BREIDER[23]), in crosses between *Limia nigrofasciata* (♀ = XX, ♂ = XY) with the 'polygenic' *L. caudofasciata*, the monogenic type of the first species is epistatic in the F_1, 'polygenic' males in small numbers occurring only in the F_2 of hybrids between *L. nigrofasciata* ♀ and *L. caudofasciata* ♂ or in the backcrosses of F_1 ♀ (*nigrofasciata* ♀ x *caudofasciata* ♂) with *caudofasciata* ♂ (Figure 2).

It is worth mentioning that the mode of polygenic (polymeric) sex-determination was found and analysed in the first line in such forms in which, besides the genetic constitution of an individual, sexual hormones contribute to the development and preservation of the sex once determined. Intersexes, as known in insects in which apparently a certain epistatic minimum in the sense of GOLDSCHMIDT is the basis of a clear-cut sex-realization, are very rare in fish, as perhaps in other vertebrates too, in which by the very early production of sex hormones (see DZWILLO[32] and YAMAMOTO[33]) the sex of an individual is strictly fixed either on a genotypical basis or simply by administration of a certain sex hormone in due time.

The building-up of a new 'monogenic' type is principally possible, of course, on the basis of polygenic (polymeric) sex-determination by a system of multiple genes (not allels!). Let us imagine that by chance two individuals, a male and a female, meet, the genetic difference between the two being assured by heterozygoty in one single pair of allels in one of them. Let us further suppose that AABBCC etc. in a homozygous condition represent a series of male determiners, then AaBBCC etc. would be the expression for a (heterogametic) female with the condition that 'a' of our formula is the expression for a very strong female tendency, so that within the frame of our classical interpretation males could be described as $M_1M_1 M_2M_2 M_3M_3$, whereas the female would be $M_1F M_2M_2 M_3M_3$, F being

Table III. Sex ratios in the progeny of *X. helleri* females, paired with two different males, one a dwarf (strong) and the other normal

Progeny of dwarf ♂		Progeny of normal helleri ♂	
♂♂	♀♀	♂♂	♀♀
32	4	–	–
15	9	–	–
11	0	5	4
1	0	–	–
46	5	19	19
Sa. 105	18	24	23

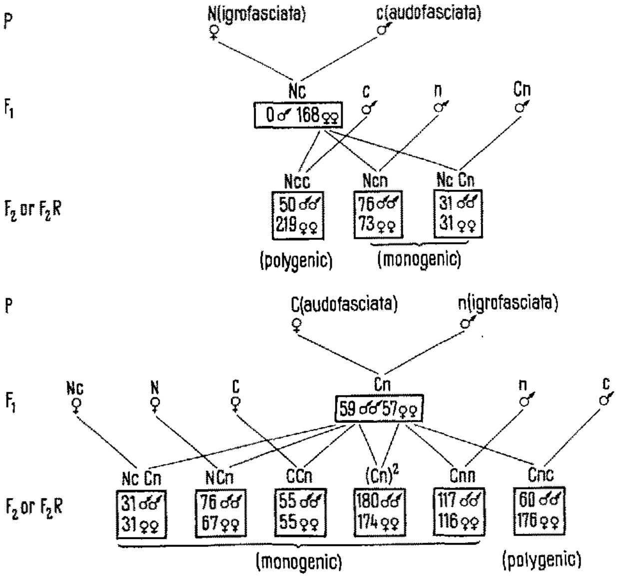

Fig. 2. Crosses in the genus *Limia*. One of the species (*nigrofasciata*) showing monogenic sex determination, the other (*caudofasciata*) being polygenic in sex determination. In the F_1-generations monogenic sex determination is epistatic, in cases of back-crossing to *caudofasciata* sex determtiinaon again becomes polygenic.

---

[32] M. DZWILLO, Biol. Zbl. *81*, 575 (1962).

[33] T. YAMAMOTO, Genetics *40*, 406 (1955).

stronger than ΣM. According to more recent results in polyploid Urodela, such an interpretation seems to be very probable (Humphrey and Fankhauser[34]). Without any doubt, in comparison with the so-called monogenic mode of sex determination, the polygenic (polymeric) one offers some difficulties on the point of its continuity from generation to generation. But as long as the gene-pool of a population is sufficiently rich to allow the formation of different degrees of strength of males and females, there is no reason to question the possibility of continuity of such a population provided that the number of its individuals is not much reduced. Under such conditions, the Sewall-Wright effect may enter into action and the population may be lost. But is this not exactly the same situation of each small population, in which a certain gene combination gained such an overweight that the plasticity of the original population was lost?

On the other hand, it has to be imagined that, in a population with polygenic (polymeric) sex determination *inter alia*, there may also occur – although rather rarely – a combination in which the sum of male determiners just equals that of female determiners, that is individuals in which, according to Goldschmidt, $\Sigma F = \Sigma M$. These combinations will certainly occur. What will be their sex and what will be their future? As far as the sex is concerned, this may depend on conditions of environmental factors realizing either the male or the female component on the basis of an equilibrium between male and female determining genes; the whole group being adjusted to gonochorism, the chances of formation of a hermaphrodite will be nil. Such a hermaphrodite due to the interaction of sex hormones being either a complete male or a perfect female phenotypically, it will mate within the population with a representative of the opposite sex which, with the greatest probability, is determined by its genotype. This is why the formation of a population of latent hermaphrodites, in which only environmental conditions are activating one side of the bisexual potency of a given individual, is very improbable.

Also in Isopods and in Amphipods, the existence of sexual hormones has been shown (Charnioux-Cotton[35], Legrand[36], de Lattin and Gross[37], de Lattin[38]). In these two orders examples of polygenic sex determination are well known (de Lattin[39, 40]) and perhaps even more pronounced than in fish. As a result of the research of many authors, especially in Isopods, species became known in which, besides females which produce very different sex ratios when combined with the same male (amphogenic ♀♀), others normally occur which produce only females (thelygenic ♀♀) or only males (arrhenogenic ♀♀). The essentially polygenic basis of these phenomena could be analysed in a number of cases. Through the investigation of Lueken[41], it became evident that, in each population of *Armadillidium vulgare*, the system of polygenes is balanced in such a fashion that its continuity is assured. On the other hand, crossing members of different and widely isolated populations results in a break-down of the more or less homoeostatic situation of each of the balanced gene pools. The research work in Isopods is hindered by some technical difficulties, e.g. small progenies, absence of colour genes for marking spermatozoa of different males, and long survival of male germ-cells in the female etc. Nevertheless, in some results the Isopods are favourable in comparison with fish.

In many other animals, the same principle of polygenic sex-determination has been found with essentially the same result. Bacci[42, 43] reported examples from marine animals, mollusca (*Patella*), annelids (*Ophryotrocha*); Battaglia[44] showed the success of selection experiments in the copepod *Tisbe*; Hauenschild[45] in a later publication accepted the same interpretation for *Grubea* (*Polychaeta*); Anders[46] found another example in the apterygot insect *Sminthurus*. Finally, Baltzer's[47] famous object *Bonellia* should be recalled. In most textbooks *Bonellia* is shown as a typical representative of so-called phenotypical sex-realization. This means that the definite sex in a larva is determined only by the decision between temporary proboscis parasitism and continuation of a free life without fixation on a proboscis of a full-grown female. In the first case, each larva is transformed into a male, in the latter into a female. But such a presentation of the data obtained by Baltzer and his students does not cover the whole affair. Baltzer[48] drew attention to the fact that, also in the presence of a female proboscis, a small number of the larvae will not become fixed and not be transformed into males. A minority of larvae in the proboscis-cultures will become young females. On the other hand, also in so-called sea-water cultures without a proboscis or extracts of a proboscis, a small number of larvae of the same set of eggs will become males. It was Baltzer who stated that these and similar results indicate the participation of a special genotypical condition in such exceptional individuals. In the terminology of polygenic sex determination, we could say: in *Bonellia* some larvae are genetically determined so strongly as females that they continue

---

[34] R. R. Humphrey and G. Fankhauser, J. Morph. *79*, 467 (1946).

[35] H. Charniaux-Cotton, C. R. Acad. Sci. Paris *240*, 1487 (1955).

[36] J. J. Legrand, C. R. Acad. Sci. Paris *238*, 2030 (1954).

[37] G. de Lattin and F. J. Gross, Exper. *9*, 338 (1953).

[38] G. de Lattin, Verhdlg. Dtsch. Zool. Ges. *1955*, 96.

[39] G. de Lattin, Z. ind. Abst.-Vererb.-lehre *84*, 1 (1951).

[40] G. de Lattin, Z. ind. Abst.-Vererb.-lehre *84*, 536 (1952).

[41] W. Lueken, Z. wiss. Zool. *166*, 251 (1962).

[42] G. Bacci, Estr. d. Publ. Staz. Zool. Napoli *21*, 183 (1947).

[43] G. Bacci, Estr. d. Publ. Staz. Zool. Napoli *26*, 110 (1955).

[44] B. Battaglia, Estr. d. Arch. Occan. e Limn. *11*, 19 (1959).

[45] C. Hauenschild, Z. Naturf. *14*, 89 (1959).

[46] A. Anders and F. Anders, Naturw. *46*, 458 (1959).

[47] F. Baltzer, Estr. d. Publ. Staz. Zool. Napoli *26*, 110 (1928).

[48] F. Baltzer, Rev. Suisse Zool. *39*, 281 (1932).

their development in the female direction even in the presence of a proboscis. Besides these strong females, there are some strong males which, even in the absence of the masculinizing proboscis substance, will become males. On the other hand, a large number of males of minor strength will be transformed in the sense of their genotypically fixed sex only under the condition that an environmental factor, namely the proboscis substance, is present in order to activate the male potencies of this type of larvae; *mutatis mutandis* are feeble females in which the genetic situation may be overthrown by the masculinizing action of the proboscis substance. Results of experiments of Herbst[49, 50], who succeeded in producing a higher percentage of males after treatment of the larvae with Cu-ions or diluted acids, are facts under the same heading. Unfortunately *Bonellia* is not a suitable object for an experimental analysis lasting for some generations, but all known facts are in good agreement with the polygenic interpretation.

Some 30 years ago, the author (Kosswig[29]) advanced the idea that in crosses of *Poecilid* fishes a certain dominant colour gene influenced the sex of its bearer in the following way: according to its genic constitution an individual would develop into a weak male, but, as the result of the addition of the colour gene to the genotype, this individual would be transformed into a female. It was supposed that the colour gene was acting as a relative realizator for femaleness, its influence on sex determination being possible only on interaction with certain feeble combinations of M-genes. Later this idea was abandoned on the basis of further research (Kosswig and Öktay[51]). It is worth mentioning that de Lattin[39] found a similar situation in two species of wood-lice. In de Lattin's cases, the feminizing effect of a dominant colour-gene within one population in nature was clearly demonstrated. Contrary to the very complex situation in species hybrids of fish, in these wood-lice the relative activity of a colour gene in the feminine direction is evident. Up to date there are no observations which could be used as an argument for the assumption that not the colour gene but merely a gene closely linked to the colour gene has the relative feminizing activity. We have to imagine that the colour gene by itself shows a pleiotropic action, controlling body colour and contributing a bit towards femaleness.

In Goldschmidt's[8] famous work on *Lymantria dispar*, the Y-chromosome was recognized as carrying the decisive F-gene (or genes). From this rare example within the complex of sex determination analysis, Goldschmidt put forward the hypothesis that this F has a predetermining character. This means that the F-gene begins to be active long before zygote formation, when the egg is still in the stage of an oocyte. In this way, the cytoplasms of all eggs receive a certain quantity of female-determining substances, these substances being of different strength, depending on the subspecies used in the experiment. Even those eggs which, as a result of the reduction division, will later lose the Y-chromosome enclosing these F-substances, the quantity of which is of fundamental importance for the development of the pure sexes or of one of the different types of intersexes in this species.

In *Isopods*, a similar situation was found by de Lattin[40] in *Cylisticus* and by Seitz[52] in *Asellus*. Although in these two forms the sex determination generally follows the polygenic (polymeric) type, there are some lines in which, under the influence of other genes, one of the female determiners (or group of strongly linked ones) begins its activity in the oocyte stage. In this way all fertilized eggs develop into females, regardless of the content of other sex-determining genes. Even such combinations of polygenes, which would have assured male development, will be transformed into females under the influence of a strongly feminizing substance in the cytoplasm as the result of predetermination. Among the many consequences of such a situation, only one may be discussed here in more detail. The absolutely feminizing substance F is transferred to all eggs, even though the gene F responsible for its production was present only in the heterozygous condition in the thelygenic female. Under such conditions, an accumulation of male-determining (M-) genes in the genotype is irrelevant and, as the final result, two genotypes may be built up: Ff MM and ff MM. The first one represents the thelygenic females, the second one males and arrhenogenic females. Whereas all eggs of thelygenic females carry F in their cytoplasm and M in their genom, only half of them have F – the other half having f. The second combination ff MM would produce males only under the condition that F is not present in the cytoplasm. This is the case when a female ff MM (which genotypically is a male) is crossed with a male with the same genic formula. In this way, starting from polygenic sex determination, the production of males and females in the ratio 1:1 is again assured, but the manifestation of male differentiation is delayed for one generation. It is worth mentioning that this type of sex-determination evolved polyphyletically within the isopods, and that it was also found in some *Diptera*; in the latter perhaps not being derived from a polygenic but merely from a 'monogenic' (XY) type of sex-determination. In the parasitic cirripedian *Peltogastrella*, two types of females exist. One is female-producing, laying small eggs, one half of which after fertilization yield female-producing females, the other half yielding male-producing females

---

[49] C. Herbst, Sitz.-ber. Heidelberger Akad. Wiss. *16*, Abh. (1929).

[50] C. Herbst, Naturw. *20*, 375 (1932).

[51] C. Kosswig und M. Öktay, Istanb. Üniv. Fen Fak. Hidrobiologie Ser. B *2*, 133 (1955).

[52] I. Seitz, Naturw. *40*, 394 (1953).

which lay larger eggs. It is interesting that, according to YANAGIMACHI[53], the female-producing females carry one extra chromosome in which a female-determining gene (or complex of genes) with a predeterminative action in the oocyte stage may be localized.

From the *Amphipoda*, some species of *Gammarus* were used in sex-determination studies. Only those may be mentioned which have a sound genetic background. In *Gammarus duebeni* and in *G. pulex* pair cultures yielded highly different sex ratios as expected on a polygenic basis (TRAUT[54]). In a strain of *G. pulex subterraneus* ANDERS[55] found a red coloured type which consisted practically only of males. Crossing of the rare red females with any male, grey or red, results again in all-male cultures, or nearly all-male cultures, whereas grey (normal) females crossed with red males yield the two sexes according to polygenic segregation and recombination. Accepting the hypothesis of colour genes as (relative) sex realizators, ANDERS gives the following explanation: In the rare red females, homozygous for the colour gene r, the constitution rr in the oocyte stage is of a predeterminative activity assuring the deposition of a male-determining substance in the cytoplasm so that, whatever the strength of female-determining genes in the later zygote may be, development is directed towards maleness. It is interesting to note that this predetermination towards maleness occurs only in oocytes homozygous for the recessive r-gene.

TRAUT[54] in *G. duebeni* found very complex genetic situations as far as sex-determination is concerned. In this species, too, sex determination follows the polygenic type; in some lines a predeterminative effect of some gene-combinations is also probable. Furthermore, an all-female strain was found in this species. In generation after generation, females of this strain produce exclusively females, but only after copulation with a male. The introduction of a gene for a somatic character from a male into the all-female line proves that the genome introduced by the spermatozoon is included in a normal zygote. Therefore reproduction in this case is bisexual, the sperma being necessary not only to assure the start of the development, as in cases of induced parthenogenesis or of merospermy. TRAUT is of the opinion that in this all-female line, a female determiner is localized in the cytoplasm as an autonomous hereditary particle (a plasma gene?) and not working by predetermination with the aid of genes of the nucleus. Isolation of individuals of this all-female strain will result in the loss of the population after one generation, its continuity is assured only if males and females of a bisexual strain are still present. In isolation there would be only one other way for the all-female line to escape dying out. This would be the 'invention' of parthenogenesis. This mode of unisexual propagation is known for some other Amphipods and Isopods, in the latter in combination with triploidy.

Zusammenfassung. Der sogenannte monogene Geschlechtsbestimmungstyp hat offensichtlich in den meisten Fällen eine polygene Grundlage. Er wirkt wie eine echte monohybride Rückkreuzung auf Grund der eigentümlichen Lokalisation der Männlichkeit und Weiblichkeit bestimmenden Gene (Realisatoren). So sind bei *Drosophila* offenbar zahlreiche F-Gene in den X-Chromosomen lokalisiert; die M-Gene dagegen liegen in den Autosomen, das Y-Chromosom ist «leer». Die quantitative Interpretation, wie sie von GOLDSCHMIDT ausgearbeitet wurde, galt lange Zeit als grundsätzlich allgemein gültig. In Wirklichkeit ist dieser Typ von Geschlechtsrealisation nur einer von zahlreichen anderen Möglichkeiten, die sich ebenfalls wieder des monohybriden Rückkreuzungsschemas bedienen. Im Gegensatz zu *Drosophila* führt bei anderen Tieren und Pflanzen das Y-Chromosom den entscheidenden Geschlechtsrealisator (Melandrium, Zahnkarpfen, Chironomiden, Säugetiere einschliesslich des Menschen). In derartigen Fällen können die Gene für das homogametische Geschlecht entweder in den X-Chromosomen oder in den Autosomen oder in beiden übertragen werden. Über ihre Anzahl können bislang keine genauen Angaben gemacht werden. Neben solchen Mechanismen, durch die ein primäres Geschlechtsverhältnis 1:1 sichergestellt wird, obwohl zahlreiche Gene dabei mitwirken können, wird in Fällen sogenannter polygener Geschlechtsbestimmung im engeren Sinne das Geschlecht auf der Basis eines polymeren Gensystems bestimmt, indem alle Kombinationen oberhalb eines bestimmten Schwellenwertes das eine, alle unterhalb desselben das andere Geschlecht bedingen. Zufällig kann unter solchen Kombinationen auch einmal ein 1:1 Verhältnis der beiden Geschlechter auftreten. In der Regel gehen aus verschiedenen Paarungen entsprechend dem jeweiligen «Stärkegrad» der kombinierten Geschlechter wechselnde Prozentsätze von Männchen und Weibchen hervor. Dieser polygene Geschlechtsbestimmungsmodus ist von *Xiphophorus helleri* und anderen Zahnkarpfen sowie von Isopoden und Amphipoden und einer grösseren Zahl anderer Wirbelloser bekannt. Auf einer polygenen Grundlage wirkt in einigen Fällen ein Farbgen als relativer Geschlechtsrealisator, wie durch DE LATTIN und ANDERS gezeigt wurde. Endlich kann dank seiner prädeterminativen Wirkung ein Gen des polygenen Komplexes die geschlechtsbestimmende Rolle übernehmen, so dass eine unisexuelle Nachkommenschaft entsteht, von der die eine Hälfte, die das prädeterminierende Gen nicht besitzt, genetisch dem entgegengesetzten Geschlecht angehört (*Cylisticus*, *Peltogastrella*).

---

[53] R. YANAGIMACHI, Biol. Bull. *120*, 272 (1961).

[54] W. TRAUT, Z. wiss. Zool. *167*, 1 (1962).

[55] F. ANDERS, Z. ind. Abst.-Vererb.-lehre *88*, 291 (1957).