THE CHROMOSOME MECHANISM AS A BASIS FOR MENDELIAN PHENOMENA.[1]

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The farther investigation proceeds, the more convincing becomes the conviction that the proportional inheritance of characters of plants and animals has its basis in the chromatin of the nucleus. The remarkable parallelism between the activities of the complicated mechanism of nuclear division and the readily predicted phenomena of Mendelian inheritance easily dispels the allurements of any other hypothesis.

When in 1897[2] the writer showed the qualitative division of the reduction or bivalent chromosomes in the megasporocyte of Lilium philadelphicum, it was even then clearly seen by a number of cytologists that such a division would have an important bearing on heredity. At the time, however, there was no way of determining in the cells of the lily studied whether the separating transverse halves of the long, twisted loops were actually individual descendants of previous univalents, and Mendelian principles and laws were still resting in the limbo of neglected scientific discoveries. The theory of qualitative division was not kindly received at the time altho the investigation on Lilium philadelphicum showed not a single important break in the series until the complete segregation of the metakinesis stage. The weight of authority both in cytology and genetics was against such an explanation. My paper was begun with the following words:— "Altho a knowledge of the changes which take place in the reduction nuclei of plants and animals is of the utmost importance, and will not doubt aid more than anything else in bringing about a correct interpretation of the facts of heredity, comparatively little has been done in this field, and the observations that have been reported disagree widely."

In 1899, Paulmier[3] reported a transverse or qualitative division for the first reduction karyokinesis while the second was represented to be equational. These results on Anasa tristis agreed with what I had observed in Lilium philadelphicum. It was one of a very few thoro investigations of the times unbiased by contrary current opinion on the subject. In June 1901, the writer published his paper on Erythronium in which a qualitative

1. Contribution from the Botanical Laboratory of the Ohio State University, No. 88.

2. SCHAFFNER, JOHN H. The Division of the Macrospore Nucleus. Bot. Gaz. 23: 430-452.

3. PAULMIER, F. C. The Spermatogenesis of Anasa tristis. Jour. of Morph. 15: 223-272.

SCHAFFNER, J. H. A Contribution to the Life History and Cytology of of Erythronium. Bot. Gaz. 31: 369-387.

division in the first reduction karyokinesis was again reported essentially similar to that described for Lilium philadelphicum. At the time this paper was written, the writer still knew nothing of Mendelian heredity. The following statement was made in regard to the probable individuality of univalent chromosomes in the bivalent chromosome—"Altho there is no way known to the writer of tracing the origin of the reduction chromosome in this nucleus to two previous ones, theoretically one might consider it possible that the reduction chromosome represents two normal chromosomes, and the closed loop the point where the usual transverse break should have taken place." Namely, when the double number of chromosomes are formed from the continuous spirem. "But such a process would necessarily result in a qualitative division."

That the bivalent chromosome is actually made up of a pair of univalents, one from the maternal and one from the paternal side, was definitely shown to be the case by Montgomery[4] in 1904. Thus the general facts of the reduction division had been worked out and there was only needed a comparison of the results with the rediscovered Mendelian heredity. Such comparisons were of course, made by many writers.

The cytological evidence may be summarized as follows: the chromosomes are self-perpetuating bodies which have a definite individuality of size and shape which can be recognized in many species. This individuality is not lost or impaired when the chromosomes spread out in the form of a network in the resting nucleus nor when they join end to end to form a continuous spirem. The haploid number of chromosomes represents a normal complement or set, each of which developes a specific attraction and unites with its corresponding or synaptic mate in the prophases of the reduction division (synapsis period) and each pair is segregated according to the law of chance to the two poles of the spindle. When at a future period gametes are formed and fertilization takes place, the univalents do not fuse but retain their separate existence during the entire zygotic stage of the organism. The pairing of corresponding univalents is of fundamental importance; for without such a process hereditary ratios would be much more complicated than what they really are, even tho the reduction division proceeded normally. The chromosomes representing synaptic mates may have absolutely similar hereditary factors and thus be homozygous and the

4. MONTGOMERY, JR. T. H. Some Observations and Considerations upon the Maturation Phenomena of the Germ Cells. Biol. Bull. 6: 137-158. See also MONTGOMERY: The Spermatogenesis of Peripatus (Peripatopsis) balfouri up to the Formation of the Spermatid. Zoolog. Jahrb. 14: 1900 and MONTGOMERY; Mitosis in Amphibia and its General Significance. Biol. Bull. 4: 259-269, 1902.

race pure in respect to all hereditary phenomena resulting from the activity of the pair, or the pair may be heterozygous in which case Mendelian phenomena must result.

Now it will be apparent that with a definite number of chromosomes whose activities during the life cycle are known it can be determined before hand just what segregations and combinations of hereditary factors are possible. If the chromosomes are the only bearers of heredity, there should not be more Mendelian segregations of two absolute, heterozygous hybrids than the permutations possible with the number of chromosomes. By an absolute, heterozygous hybrid is meant one in which all the univalent chromosomes have at least one distinctive factor. So

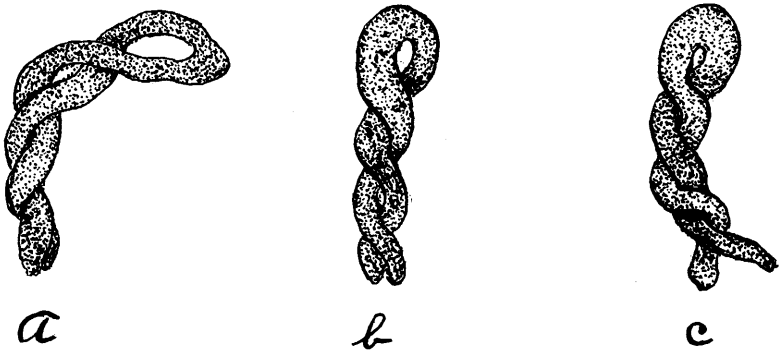

Fig. 1, a, b, c. Bivalent or reduction chromosomes from a megasporocyte of Lilium philadelphicum. The two longitudinal limbs of the twisted loop represent two univalent chromosomes, one maternal and one paternal, fused end to end in synapsis and folded lengthwise, the synaptic joint being at the head of the loop. Each univalent has already divided longitudinally into two daughter chromosomes but these are not evident in the figures which were taken from a preparation stained with a rather diffuse stain. It was this type of chromosome which first lead the writer to the conclusion that the reduction division is a qualitative division. The true nature of the formation and division of these chromosomes can only be determined by studying the preceding and subsequent stages.

far as the writer knows, the possible segregations of distinct combinations have never been tested practically. In Canna (as will appear below) which is said to have but six univalent and three bivalent chromosomes, there would be twenty-seven possible varieties from two original pure lines without considering possible new characters which might appear as the result of the activity of a heterozygous pair. This is perhaps the best plant on which the theoretical expectation might be tested out. Unfortunately many of the varities produce little or no seed. The hybridization would have to be carried on between varieties giving completely fertile offspring.

Now we can make the following possible hypotheses in regard to heredity:

1. All the hereditary factors are in the cytoplasm and other protoplasmic structures outside of the chromosomes.
2. Part of the hereditary factors are in the chromosomes and part in the protoplasm outside of the chromosomes, especially in centrosomes and plastids.
3. All the hereditary factors are resident in the chromosomes.

The last hypothesis still seems to explain all known hereditary phenomena. It is probable, however, that all protoplasmic structures have hereditary factors. Nevertheless, we can safely say that all normal Mendelian heredity must have its factors in the chromosomes alone.

Now it may easily be true that certain hereditary factors may be resident in all of the chromosomes of a haploid set, and if the synaptic haploids also contained the factor, it could not be segregated out in reduction. Fundamental characters may be of this nature. A loss of part of the nucleus would not result in a loss of essential factors. The factor may be in all but one of the haploid set, all but two, etc., and finally in but one chromosome. We can conceive that new trivial or superficial factors commonly originate in but one chromosome or in one synaptic pair and that later the property might be acquired by other chromosomes of the set. If only one chromosome contains the factor, the simplest kind of Mendelian phenomena will result, in breeding distinct varities.

It is self evident that each chromosome and probably each of its component organs contains many hereditary abilities or factors. If two definite factors, each of which can produce a distinct character, are in the same chromosome, the factors and characters must be always linked until the chromosome breaks up abnormally into new units or individuals. Such, apparently chromosome-linked factors are well known.

Fundamentally, entirely independent of chromosome synapsis and segregation are the phenomena of dominance and recessiveness. These show a similarity to activity and latency of factors as observed in the ordinary growth and life cycle. These phenomena have nothing to do with our chromosome hypothesis except in so far as dominant and recessive factors may be shifted from one heredity set or combination to another. Dominance and recessiveness should come under possible control like latency and activity. Dominance and recessiveness when compared to activity and latency of factors do not decidedly indicate presence and absence. From the standpoint of the chromosome hypothesis a recessive factor may be either an absence or a presence. The whole problem of the influences which cause, modify, or prevent

the expression of a character from a specific factor is one which presents a marvelous field for investigation and experimentation. The influence of the ordinary ecological factors has been studied to some extent but not from the exact standpoint of the systematist and geneticist. One need only consider the remarkable structures developed in certain insect galls to be impressed with the fact, that specific characters can be developed without any previous phylogeny of the character in relation to the factor being involved. It is evident that the same factors may give rise to very diverse types of characters, when their immediate environment is changed. The influence of the sexual condition and one factor or set of factors on another may come under the same general category of environmental influences determining expression.

On the hypothesis that the chromosomes contain the hereditary factors, the possible number of gametes and zygote combinations, giving rise to diploid individuals is given below. These results must necessarily follow according to the law of chance so long as the chromosomes retain their individuality, pair as synaptic mates in reduction, and segregate and combine according to the law of probablity.

Let x = number of chromosomes.

If x = 1 and 2x = 2;

And chromosomes a ♦ — ♦ n

Then gametes { eggs or sperms } = a n

Possible combinations = 4.

aa an na nn

Hereditary constitutions = 3

a_2 an n_2

If x = 2 and 2x = 4

Chromosomes a ♦ — ♦ n

b ♦ — ♦ o

Gametes { eggs or sperms } = a a n n / b o b o

Possible combinations = 16, as follows:

abab	aoab	nbab	noab
abao	aoao	nbao	noao
abnb	aonb	nbnb	nonb
abno	aono	nbno	nono

Cancel similar constitutions and there are 9 combinations as follows:

a_2b_2	anbo	n_2b_2
a_2bo	a_2o_2	n_2bo
anb_2	ano_2	n_2o_2

If x = 3 and 2x = 6;

Chromosomes a ♦ — ♦ n
b ♦ — ♦ o
c ▼ — ▼ p

The following types of gametes are possible, either male or female:

a	a	a	n	a	n	n	n
b	b	o	b	o	b	o	o
c	p	c	c	p	p	c	p

Possible combinations = 64

Cancel similar ones and there are left 27 types of chromosome constitutions.

$a_2b_2c_2$	ano_2c_2
a_2b_2cp	ano_2cp
a_2boc_2	$n_2b_2c_2$
anb_2c_2	n_2b_2cp
a_2bocp	n_2boc_2
anb_2cp	n_2bocp
$anboc_2$	$a_2o_2p_2$
anbocp	ano_2p_2
$a_2b_2p_2$	$n_2b_2p_2$
a_2bop_2	n_2bop_2
anb_2p_2	$n_2o_2c_2$
$anbop_2$	n_2o_2cp
$a_2o_2c_2$	$n_2o_2p_2$
a_2o_2cp	

If x = 4 and 2x = 8;

Chromosomes a ♦ — ♦ n
b ♦ — ♦ o
c ▼ — ▼ p
d ● — ● q

The following gametes are possible.

a	a	a	a	n	a	a	a	n	n	n	a	n	n	n	n
b	b	b	o	b	b	o	o	b	b	o	o	b	o	o	o
c	c	p	c	c	p	p	c	p	c	c	p	p	c	p	p
d	q	d	d	d	q	d	q	d	q	d	q	q	q	d	q

In this case 256 types of matings are possible giving rise to 81 varieties of hereditary constitutions.

If x = 5 and 2x = 10;

Chromosomes a ♦ — ♦ n
b ♀ — ♀ o
c ▼ — ▼ p
d ● — ● q
e ■ — ■ r

The following gametes are possible:

a	a	a	a	a	n	a	a	a	n	a	a	n	a	n	n
b	b	b	b	o	b	b	b	o	o	b	o	b	o	b	b
c	c	c	p	c	c	c	p	p	c	p	c	p	c	c	c
d	d	q	d	d	d	q	q	d	d	d	q	d	d	q	d
e	r	e	e	e	e	r	e	e	e	r	e	e	r	e	r

a	a	n	a	n	n	a	n	n	n	a	n	n	n	n	n
o	o	b	o	b	o	b	b	o	o	o	b	o	o	o	o
p	p	p	c	p	c	p	c	c	p	p	p	c	p	p	p
q	d	q	q	d	q	q	q	d	d	q	q	q	d	q	q
e	r	e	r	r	e	r	r	r	e	r	r	r	r	e	r

From these 1024 combinations are possible, representing 243 constitutions.

If x = 6 and 2x = 12;

64 kinds of male or female gametes possible,
4,096 chance combinations,
representing 729 hereditary constitutions.

If x = 7 and 2x = 14;

128 kinds of gametes possible,
16,384 combinations,
representing 2187 constitutions.

If x = 8 and 2x = 16;

256 kinds of gametes,
65,536 combinations,
representing 6561 constitutions.

If x = 9 and 2x = 18;

512 kinds of gametes possible,
262,144 combinations,
representing 19,583 constitutions.

If x = 10 and 2x = 20;

1,024 kinds of gametes possible,
1,048,576 combinations,
representing 58,749 constitutions.

If x = 11 and 2x = 22;
2,048 kinds of gametes possible,
4,194,304 combinations,
representing 176,247 constitutions.

If x = 12 and 2x = 24;
4,096 kinds of male or female gametes possible,
16,777,216 combinations,
representing 528,741 actual constitutions, or over half a million.

The presence of an allosome, which may contain hereditary factors, complicates the results of Mendelian segregation and probably is the cause, at least in many cases, of sex-limited characters. That the factors are not to be regarded as sex-linked becomes obvious in such a case as color-blindness in man. For there are both color-blind men and women, but thru the reduction mechanism by which the allosomes are segregated and the new combinations brought about during fertilization, thru the influence of the sex determination of the egg, it happens that many more males show the color blind character than females. If we assume differential attraction between eggs and sperms and if there is an accessory chromosome or allosome in man and if the factor for color-blindness is associated with this chromosome, then it would follow that a color blind man mated with a normal woman could have no color-blind children because the two types of eggs would be normal and the egg determined as female would attract the sperms containing the allosome (i. e. having the color-blind factor) and this would give but a single dose which is not sufficient to produce the color-blind character in the female. The egg determined with male condition would attract only sperms without the allosome; therefore, all the males would be normal, but the color-blind female having a double dose would produce eggs, all of which, whether determined as male or female, would have the color-blind factor in the allosome, and if mated with normal, the sons would all be color-blind, because a single dose produces the color-blind character under the influence of the male condition. The daughters would be normal having only a single dose, which as stated, is not sufficient to develop the color-blind character in the presence of the female condition in the cells of the body. These suppositions agree with the observed facts. It also comes about that in hybridizing individuals, which may have a specific factor in the allosome, different degrees of the character may be shown because a double dose may give a greater degree of the character than a single dose. If the male

has one allosome and the female two, the highest efficiency character may appear to be transmitted only thru the male simply because the female cannot get the double dose of favorable allosomes except from a male. It is probable also that there are sex-limited characters whose factors are not in the allosome. In such cases the male of female condition modifies the activity of the factor.

Besides the segregating results due to normal cell divisions there is, of course, the possibility of irregular segregations and the fusion of parts of one chromosome with another. Irregularities in reduction and vegetative karyokineses may thus produce fundamental changes in heredity. Irregularities may be of three general types.

a. The chromosomes may be doubled from the previous number of the species, probably thru failure of a reduction division.

b. Increase or decrease of the usual number may be brought about by some of the chromosomes being left behind on the spindle, or by the entire synaptic pair or the daughter halves being pulled to one pole.

c. Material from one chromosome may possibly be transferred to another when fused ends of two univalents are pulled apart in the reduction metakinesis and material belonging to one chromosome might also be detached and drawn into another during the protochromosome stage of reduction.

The question of the origin of an hereditary factor in a chromosome or the absolute loss of a factor involves a consideration of the mechanism, and the chemical, physical and vital properties of the chromosomes about which we know little or nothing at the present time. But that the chromosome itself is a mechanism apparently as complex in its own way as the nucleus itself is revealed by the microscope even with present methods. What further complications may exist until the larger chemical units are reached can only be conjectured. There is also a possibility that the mosaic arrangement of the chromosomes in the zygote may influence the expression of hereditary factors and the arrangement and adjustment of chromatin granules and any other structures present in the linin plasm may have something to do with the peculiar hereditary properties or abilities manifested by living matter.

SUMMARY.

The normal hereditary mechanism then of the chromosomes acts as follows:

1. The chromosomes normally function as individuals and are segregated as such at each karyokinesis.

2. The chromosomes do not conjugate or fuse, nor does their material mix in the fertilization stage; but each chromosome is carried thru the zygote stage of the organism as a definite individual.

3. In the reduction division, the chromosomes show themselves to be definitely paired; and the 2x number of the zygotic individual represents two definite sets or complements of chromosomes, each one of the one set having its corresponding synaptic mate in the other. A specific attraction develops between each pair of synaptic mates during the prophases of reduction resulting in an end to end fusion in pairs and a subsequent folding side by side, so that a bivalent chromosome represents synaptic univalents fused longitudinally at least in the ordinary elongated types of chromosomes.

4. The segregation of the univalents during reduction is according to the law of chance; therefore, each daughter cell receives a full (x) complement of univalents, some of the set being descendants of those brought into the zygote by the parent egg and some by the sperm.

5. These processes are in harmony with the observed phenomena of Mendelian heredity.

CORRECTION

The list of Insect Galls of Cedar Point (Ohio Naturalist, December, 1914) is in error as follows:

P. 381—**Andricus futilis** O. S. should doubtless be **Dryophanta papula** Bassett.

P. 382—**Holcaspis globulus** Fitch was found on **Quercus macrocarpa** instead of **Q. imbricaria.**

I am indebted to Mr. L. H. Weld of Evanston, Ill., for these corrections.

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