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THEORETICAL PAPERS AND REVIEWS

To the memory of the prominent cytogeneticist Aleksandra Alekseevna Prokofyeva-Belgovskaya on the 100th anniversary of her birth

Variation and Evolution of Meiosis

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Abstract—Meiosis arose in the evolution of primitive unicellular organisms as a part of sexual process. One type of meiosis, the so-called classical type, predominates in all kingdoms of eukaryotes. Meiosis is controlled by hundreds of genes, both shared with mitosis and specifically meiotic ones. In a wide range of taxa, which in some cases include kingdoms, meiotic genes and features obey Vavilov's law of homologous variation series. Synaptonemal complexes (SCs) temporarily binding homologous chromosomes at prophase I, ensure precise and equal crossing over and interference. SC proteins have 60–80% homology within the class of mammals but differ from the corresponding proteins in fungi and insects. Thus, nonhomologous SC proteins perform similar functions in different taxa. Some recombination enzymes in fungi and plants have common epitopes. The molecular mechanism of recombination is inherited by eukaryotes from prokaryotes and operates in special compartments: SC recombination nodules. Chiasmata, i.e., physical crossovers of nonsister chromatids, are preserved in bivalents until metaphase I due to local cohesion of sister chromatids in the remaining SC fragments. Owing to chiasmata, homologous chromosomes participate in meiosis I in pairs rather than individually, which, along with unipolarity of kinetochores (only in meiosis 1), ensures segregation of homologous chromosomes. The appearance of SC and chiasmata played a key role in the evolution of unicellular organisms since it promoted the development of a progressive type of meiosis. Some lower eukaryotes retain primitive meiosis types. These primitive modes of meiosis also occur in the sex of some insects that is heterozygous for sex chromosomes. I suggest an explanation for these cases. Mutations at meiotic genes impair meiosis; however, due to the preservation of archaic meiotic genes in the genotype, bypass metabolic pathways arise, which provide partial rescue of the traits damaged by mutations. Individual blocks of genetic program of meiotic regulation have probably evolved independently.

INTRODUCTION

The studies of meiosis conducted in the 20th century have revealed numerous examples of similarity of this process in members of close and distant taxa: protists, fungi, plants, and animals. In particular, gametic, zygotic, and intermediate types of meiosis display striking similarity of cytological events essential for prophase I, which is a crucial and most complex meiotic phase [1, 2]. This similarity can only be explained by the fact that, as early as in the epoch of unicellular organisms, evolution has singly (or repeatedly, as discussed below) created a successful cellular mechanism of alteration of the diploid and haploid phases of development, and this mechanism became predominant (but not the only one) in eukaryotic organisms.

SPECIFIC MEIOTIC GENES

Both mitosis and meiosis are genetically controlled. Some of these genes are shared by mitosis and meiosis while others are specific for each of these modes of cell division. Historically, the first specific meiotic gene discovered was *crossover suppressor of Gowen, C(3)G*, found in *Drosophila* in 1922 [3]. Since then, the number of specific meiotic genes (mei genes) detected has been progressively increasing and by 2000 reached approximately 360 in *Saccharomyces cerevisiae* (which is best-studied in this respect) [4] and 82 in *Drosophila melanogaster* [5]. The difference between the number of meiotic genes in these two organisms is probably explained not by differences in their genetic control of meiosis but by the fact that, due to objective reasons, the understanding of molecular genetics of this process is far better in unicellular yeast than in *Drosophila* and other multicellular organisms.

Models for investigation of mei genes, apart from *S. cerevisiae*, include in fungi ascomycetes (*Schizosaccharomyces pombe, Ascobolus, Sordaria macrospora, Neurospora crassa*), basidiomycetes (*Coprinus lagopus* and *C. cinereus*) and in flowered plants maize, tomato, rye, and *Arabidopsis thaliana.* Genetics of meiosis in mammals including human is for obvious reasons far less understood.

An analysis of primary issues of cytogenetics and genetics of meiosis covering all eukaryotic kingdoms and including more than thousand references was published by Zickler and Kleckner [6], while Grishaeva

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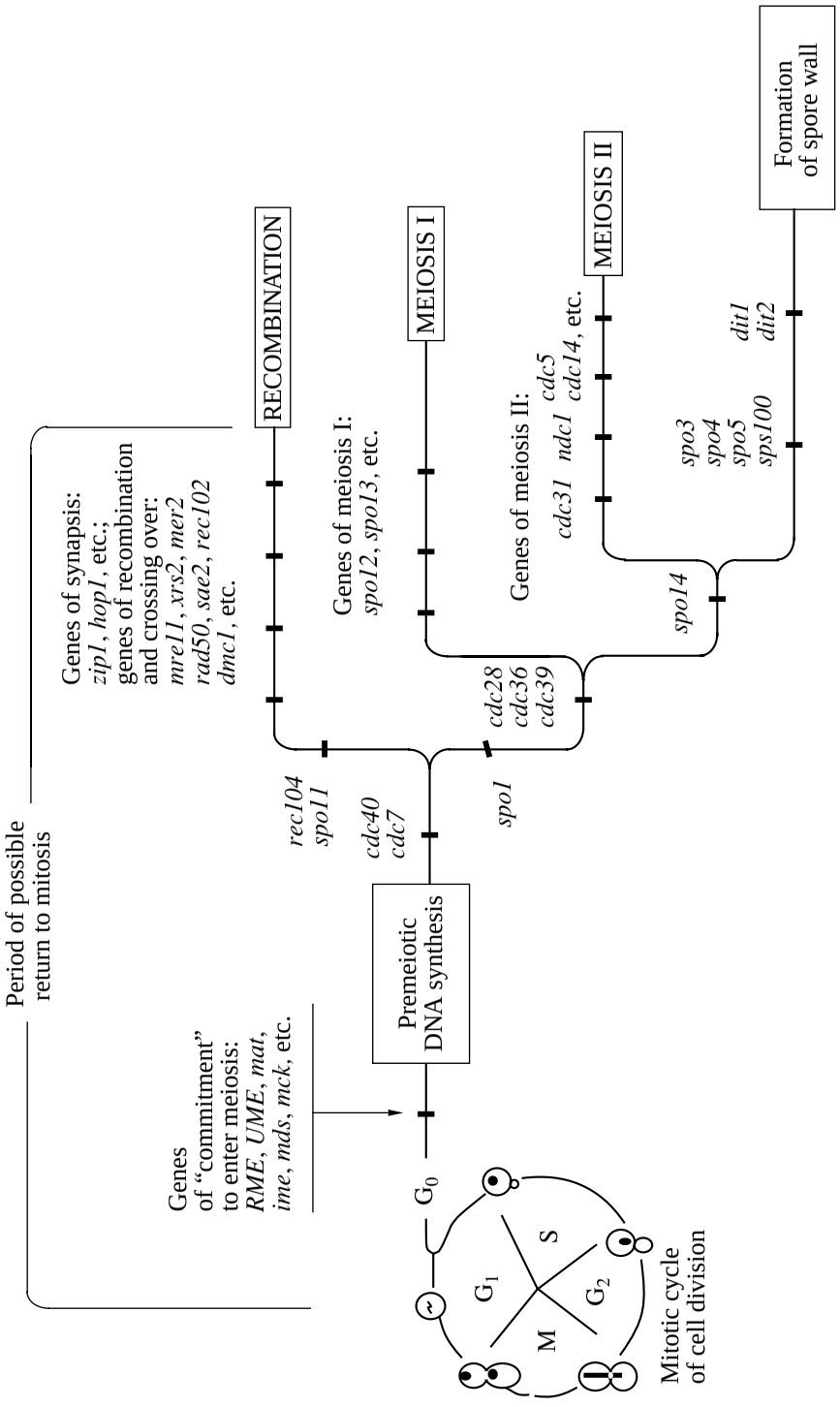

Fig. 1. Scheme of events upon the transition from mitotic to meiotic division in budding yeast *Saccharomyces cerevisiae*. Symbols of some genes regulating the transition and major steps of meiosis are given (after personal communication of R. Esposito, 1995; abridged).

and Bogdanov reviewed the information on mei genes in *D. melanogaster* [5].

The cycles of mitosis and meiosis in yeast *S. cerevisiae* are schematically shown in Fig. 1. These unicellular organisms pass from mitosis to meiosis on starvation (nitrogen lacking) medium [7]. Under these conditions, the gene cascade of "commitment to meiosis" are activated. As seen in Fig. 1, the passage by the cells of the checkpoint of irreversibility of meiosis switches on first genes of chromosome synapsis and recombination, then genes of kinetic phases of divisions I and II, and, finally, genes of sporulation proper.

HOMOLOGY OF GENES AND TRAITS OF MEIOSIS

The phenotypic expression of mei genes in yeast is similar to that in other fungi and higher plants. Undoubtedly, genes that control (or can control) analogous or homologous meiotic traits will be discovered in *Drosophila* and other higher plants. For instance, meiotic gene mutations of *Arabidopsis* similar in phenotypic expression to the previously detected mutant meiotic genes of maize, rye, tomato, and even *S. cerevisiae*, have been discovered since 1995 using effective insertion mutagenesis (see [4, 8]). In many cases, the products of the predicted genes must be (and in fact are) specific meiotic proteins: enzymes of meiotic recombination, structural chromosome proteins, proteins of kinetic meiotic machinery [4, 8].

Thus, meiotic traits in close and distant taxa obey Vavilov's law of variation in homologous series. Vavilov established this fundamental biological concept first for plants and then extended it to animals. In the brief formulation of 1930, homologous variation series are described by Vavilov as "the biological concept consisting in the existence in different plant and animal species and even genera of repeated, analogous, parallel series of forms, i.e., forms similar in morphological and physiological traits" [9]. In the third (1935) edition of his work included in [9], he stated that these regularities are also valid for higher taxa, such as families and classes, and gave examples of homology of these processes in asco- and basidiomycetes, within the class of ciliates, in fossilized mollusks, insects, amphibians, and mammals. In the 1960s, based on the development of molecular biology in the 1950s–1960s, Vorontsov [10] extended the use of Vavilov's law by considering the nucleotide code of protein synthesis as the material basis of homology of genes and traits. In his article, Vorontsov discusses the issues of (1) molecular and cellular bases of homology and reverse mutation; (2) homology of genotypes and homology of traits; (3) reversibility of traits and irreversibility of evolution; (4) monophily and the possibility of a parallel appearance of supraspecific taxa; (5) homology at different levels in different organs of one organism. This publication also concerned large-scale evolutionary events, such as aromorphoses, which are discussed below. Takhtadzhyan [11], Timofeeff-Ressovsky *et al.* [12], and other authors [13, 14] considered these issues in light of the more recent advances of the evolutionary theory. Thus, it became clear that the law of homologous series of hereditary variation applies to a wide range of organisms at all levels of organization of the living matter. In particular, it can be applied to the traits of meiosis at the cellular level and can be used in analysis of variation and evolution of meiosis.

I would like to list several examples showing that meiosis in plants of close and distant taxa obey the law of homologous series. For instance, a radiation-induced mutant with shorter and denser than normal chromosomes at meiotic metaphase I was found in barley *Hordeum vulgare* [15]. In mitosis chromosomes of this mutant preserved normal length and the extent of chromatin compaction. Consequently, this mutant trait was strictly specific for meiosis. Later, Sosnikhina *et al.* [16, 17] found a phenotypically homologous meiotic mutation *mei10* in rye *Secale cereale*; these authors are currently maintaining an inbred line that segregates these mutants. Thus, cereal species barley and rye have phenotypically homologous meiotic mutations (and genes). Another example concerns taxonomically distant species: maize *Zea mais* [18] and onion *Allium fistulosum* [19]. In these species, meiotic mutations revealed that, in addition to normal synapsis, exhibit indiscriminate (partially heterologous) synapsis, i.e., synapsis of nonhomologous chromosome at meiotic prophase I. In our laboratory two independent mutations of this type, *sy7* and *sy10*, were isolated in inbred rye lines from Sosnikhina's genetic collection [20, 21]. Then the series of indiscriminate synapsis mutants of rye was extended posing the question of their allelism [22]. These mutations were at first assigned to the category of mutations of premature chromosome desynapsis at late meiotic prophase I. However, an electron microscope study of synaptonemal complexes showed that the mutations affect an earlier stage of meiosis, namely, the process of mutual recognition of homologous chromosome loci at early prophase I [22, 23]. The phenotypic expression of the mutations has been also similarly revised in other meiotic genes of various organisms [4, 23]. Below, we return to the problem of homology and analogy of different meiotic genes and traits.

Another interesting example of homology in a major meiotic trait in fungi, plants, and animals is as follows. Until the late 1970s, all reviews and textbooks stated that, in contrast to fungi and animals, meiosis in plants lacks "chromosome bouquet" at early prophase I (as it lacks centrioles and spindle polar bodies), and chromosomes are brought together from large distances by a mechanism of sinesis, that is, compression of chromosomes into a bundle or knot. In the late 1970s, Gillies and later other authors discovered this bouquet of synaptonemal complexes on the ultrathin sections of meiotic cells of maize and rye. It turned out that the chromosome bouquet (clustering of telomeres on the nuclear membrane) is characteristic of all plants (see

[24]). Recently, elegant evidence was obtained for genetic control of the chromosome bouquet formation at leptotene and zygotene of meiosis in rye [25]. It is known that yeast also have a gene coding for a telomeric chromosome protein whose function mediates clustering of chromosome telomeric regions at the inner surface of the nuclear membrane (Trelles-Sticken *et al.*, cited from [26]; see also [24]). Thus, chromosome clustering on the nuclear membrane at early meiotic prophase I and the ensuing organization of the prophase meiotic chromosomes in a bouquet is characteristic of all kingdoms of eukaryotes. Apparently, this is an ancient trait of meiosis. This complex trait is likely to have polygenic control. I have no information as to homology of the genes for this trait in yeast and higher plants. Therefore, at the present stage of knowledge we can only speak of functional analogy of these genes, which results in the trait homology in Vavilov's sense, i.e., phenotypic homology of the trait in different eukaryotic kingdoms. In animals, this trait was discovered by cytologists as early as at the end of the19th century, while in plants it was found only in the last quarter of the 20th century. This trait of prophase I is discussed in detail in the review by Zickler and Kleckner [24]. An example of similar phenotypic homology provided by the same function of genes whose primary structures are not homologous is considered in section "Synaptonemal Complex."

ESSENTIAL DIFFERENCES BETWEEN MEIOSIS AND MITOSIS

Cytological events underlying key differences between meiosis and mitosis are controlled by three groups of genes. These are genes for synapsis and recombination of homologous chromosomes at meiotic prophase I and genes of kinetic machinery of meiosis I. Genes of synapsis and recombination closely interact but they nevertheless differ in the elementary expression at the cellular level and in the evolutionary history.

Consider the classical scheme of meiosis as compared to that of mitosis (Fig. 2). Here I begin this description with the culmination of each cell division, metaphase (Fig. 2b) rather than with the early stages of mitosis as is generally done in textbooks. In mitosis, the chromosomes consisting of two sister chromatids each are arranged on the equatorial plane of the division spindle. They are held in place by two forces: the tension of the spindle chromosome threads pulling toward the pole and the sister chromatid cohesion in the centromere region. At metaphase the kinetochore is already doubled, and, after the degradation of the cohesin protein, sister chromatid cohesion disappears and the spindle microtubules bring sister chromatids to the poles.

At metaphase I of the first meiotic division (meiosis I), sister chromatid cohesion is also present and even enhances (in *D. melanogaster* this is controlled by the meiosis-specific gene *ord* producing a meiosis-specific protein, cohesin). However, there are two more factors determining specific features of meiotic metaphase I: (1) chiasmata that link homologous chromosomes into bivalents and (2) unipolarity of kinetochores resulting from the fact that the doubled kinetochores do not divide in meiosis I staying linked.

Chiasmata, i.e., physical manifestations of nonsister chromatid crossovers in homologous chromosomes, are produced by crossing over. Crossing over occurs at meiotic prophase I but its consequences essential for meiosis manifest at metaphase I and anaphase I. As a result of this process, one chromatid of each chromosome exchange segments with a nonsister chromatid of the homologous chromosome. Due to crossing over, these segments (shown as solid and open in Fig. 2b) become linearly attached to nonsister centromeres (and kinetochores) rather then their own ones, but stay in lateral cohesion with their sister chromatids. Chiasma is exactly this construction consisting of two crossover nonsister chromatids, each of which remain linked by cohesion with its sister chromatid (box 2 in Fig. 2b). At metaphase I chiasmata counteract the pulling tension of the spindle and retain the bivalents at the spindle equator until the degradation of meiosis-specific protein cohesin that links chromatids in the chiasma region. The proteolytic cleavage of cohesins, which hold chromatids together, and the genetic control of this meiotic process are studied in detail in several organisms with special attention given to *S. cerevisiae* [27, 28].

Due to the pairwise arrangement of homologous chromosomes at the spindle equator and the features of chiasmata and kinetochores described above, only homologous chromosomes segregate at meiotic anaphase I (Fig. 2b).

Incomplete doubling (nondisjunction) of kinetochores in *S. cerevisiae* is caused by the fact that gene *CDC31*, whose product is essential for effective kinetochore splitting in mitosis, in meiosis I is temporarily suppressed by the product of other meiosis-specific gene, *SPO13*. In the second meiotic division, gene *SPO13* does not function, its protein product is consumed, the arrest of *CDC31* operation is lifted, and sister chromatids can move to the poles as in mitosis [29]. In meiotic metaphase I of *D. melanogaster*, this suppression of kinetochores is effected by gene *mei-S332* [30], and the function of meiosis-specific sister chromatic cohesion is fulfilled by the protein product of gene *Ord* [31]. Yeast gene *SPO13* lacks structural homology with the *Drosophila mei-S332* gene as well as with any gene of *Drosophila*. Thus, we observe phenotypic homology (homologous function) of specific meiotic genes, *SPO13* and *mei-S332*, in extremely distant groups of organisms, fungi and insects. This is a striking example of convergence of a fundamental cellular function based on proteins that are different in the primary structure but have the same function in the cell.

Summarizing the description of the genes controlling kinetic meiotic stages, genetically controlled

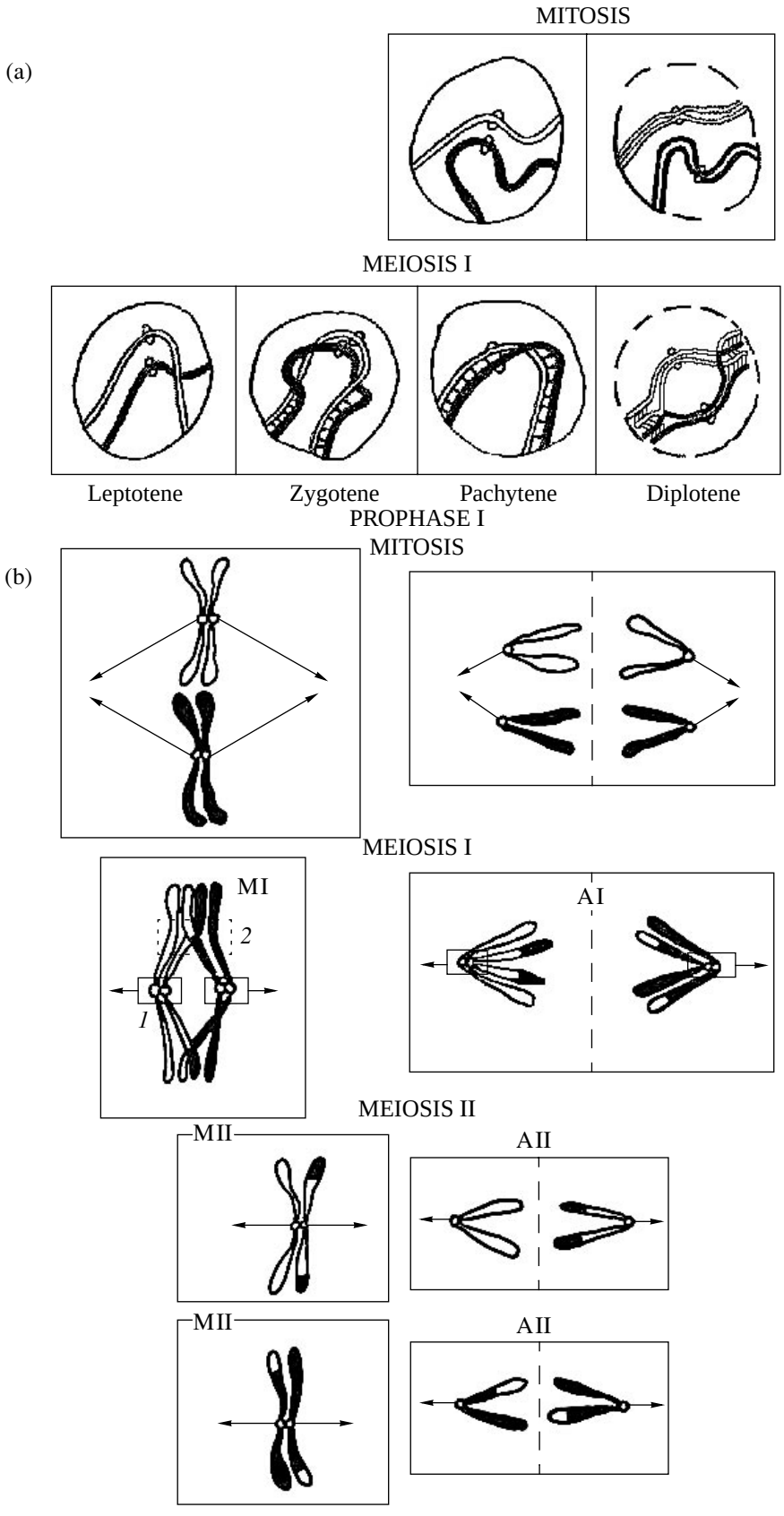

Fig. 2. Schemes of mitosis and meiosis. Box *1* indicate the centromeric chromosome region carrying a nondisjuncted kinetochore. Box *2* indicate a chiasma. See text for further explanations.

events—chiasmata and kinetochore unipolarity—provide meiotic segregation at anaphase I not of sister chromatids (as in mitosis) but of homologous chromosomes, each of which consists of two sister chromatids.

THE RELATIONSHIP BETWEEN DNA REPLICATION, CROSSING OVER, AND CHIASMATA

For several decades the relationship stated in the heading to this section has been the subject of discussion reflected in genetic textbooks and manuals. By the early 1990s, the dispute on the validity of speculatory hypotheses ("classical" theory of crossing over by Saks or the theory of "partial chiasmotypy" by Jansens and Darlington, see [32]) became history as well as the question on the participation of chromosome replication in crossing over.

The modern views on the cellular events prior to and during prophase I of classical meiosis confirmed by a plethora of experiments and coordinated by the world scientific community at regular conferences on meiosis is as follows [4, 24, 33]. (1) At premeiotic interphase and early leptotene, meiosis-specific endonucleases cause numerous double-strand DNA breaks (DBSs). (2) Concurrently, local mutual recognition of individual loci and their pairing is observed. DSBs are the first stage of the multi-stage process of genetic recombination, which is completed only at the end of pachytene. (3) At late premeiotic interphase and during leptotene, the clustering of centromeric chromosome regions typical of somatic cells disappears. It is succeeded by the clustering of telomeric chromosome regions and the formation of the chromosome bouquet characteristic of early meiotic prophase I. The spatial organization of chromosome in the bouquet promotes bringing together of homologous chromosomes from large distances to those of the order of 300 nm and the alignment of the parallel segments of these chromosomes. (4) At zygotene, the formation of synaptonemal complexes (SCs) starts between homologous chromosomes. In plants, SCs are formed polylocally, and these loci are more densely grouped in subtelomeric chromosome regions. In many animal species, the SC formation in each arm occurs unidirectionally, from the telomere to the centromere. (5) The SC formation occurs in parallel with the DSB processing (particularly, with the formation of Holliday junctions) mediated by RecA-like proteins, enzymes Rad51 and Dmc1 (epistatic group of the *RAD52* genes in *S. cerevisiae*). These proteins are localized in the special SC compartments, the so-called early meiotic nodules. A disruption of the function of these enzymes (e.g., by mutation) arrests the SC elongation. Meiotic recombination follows the scenario of molecular events described by Szostak *et al.* [34]. (6) The completion of the SC formation along the total length of the bivalents corresponds to the onset of pachytene. The pachytene stage includes the final events of recombination, i.e., implementation of the recombination events in crossovers or gene conversion. These events are controlled by a specific group of genes. Their protein products, recombination enzymes, are grouped in the late recombination nodules of SC (see below). (7) At diplotene, the SC is being gradually destroyed, the sister-chromatid cohesion disappears, chiasmata resulting from crossing over become visible under a microscope. (8) During metaphase I, homologous chromosomes attached in bivalents by chiasmata are cooriented toward different poles at the equatorial plane of the division spindle. (9) During anaphase I, homologous chromosomes separate whereas complete segregation of recombined recessive and dominant alleles occurs only at anaphase II.

Summarizing, the initiation of homologous synapsis (the SC formation) and the early stages of recombination are strongly associated in space and time; an arrest of one of these processes blocks the other, and vice versa; chiasmata result from crossing over.

SYNAPTONEMAL COMPLEX

Synaptonemal complex is a meiosis-specific subcellular (subchromosomal) structure. At pachytene, the SC joins the homologous chromosomes positioned in the nucleus in parallel with each other. The SC formation is necessarily required for forming chiasmata. The term conjugation used in Russian publications and textbooks is considered obsolete in international literature. It has been replaced by the term synapsis (close contact). This term is employed to describe lateral joining of chromosomes by the SC. Another term for this is pairing. In the narrow sense, pairing means local joining of chromosomes at premeiotic interphase and leptotene (see above). Sometimes this term is used in a wider sense, namely, to designate pairwise joining of homologs in general and joining of homologs as bivalents at diakinesis and metaphase I in particular.

The SC was discovered in the 1950s [35, 36], at the time that could justly be called the age of great discoveries in electron microscopy. The SC role in meiosis has been extensively studied (see [6, 24, 37–42] for review). A model of the organization of the eukaryotic chromosome connecting the SC structure and function with the organization and functioning of the chromosome was proposed by Stack and Anderson [43].

The SC exists only during meiosis and only for a short period in the life of the meiotic cell. It starts forming at meiotic zygotene and is gradually degraded at diplotene after having completed its function [44, 45].

Functions of the Synaptonemal Complex

It is generally believed that the SC is necessary for forming chiasmata. Lower eukaryotes lacking chiasmata, e.g., *S. pombe* and *Aspergillus nidulans*, also lack the SC [33]. Even more importantly, the SC is required for crossover interference. Both *S. pombe* and *A. nidulans* lack crossover interference. Mutants *zip1* of *S. cer-*

evisiae with defective SC formation also do not exhibit crossover interference (but have crossing over) [46]. Interference of crossing over and chiasmata in mouse and maize reduces and even becomes negative in a local region of the bivalent, particularly near the breakpoint of one of the homologs that underwent inversion or reciprocal translocation, i.e., at the place where pairing partners change and the SC integrity is disrupted ([47, 48] and other references).

It is not quite clear why the SC determine crossover interference. The SC contains recombination nodules that accumulate recombination enzymes. It may be that these nodules cannot be located closer to each other than the distance of interference. If the SC continuity is disrupted, the reading of distance starts anew after the gap.

In addition to the established role of the SC in mediating crossover interference, this structure may have another, hypothetical function. The SC may be required to ensure the possibility for paired homologous chromosomes to separate at anaphase I rather than be attached irreversibly as in *Drosophila* salivary gland cells [40, 49]. This hypothesis does not contradict the SC role in synapsis, crossing over and chiasma formation. It can be tested by an experiment the results or predicted consequences of which could be checked. At the present level of knowledge, it can be assumed that the synapsis reversibility might be the primary function of the SC while its role in crossing over and chiasma formation is a consequence, but this remains to be proven.

The Formation of Synaptonemal Complexes

The SC is formed from the axial cores of homologous chromosomes (Fig. 3a). These axes are also specific for meiotic chromosomes and only at the stage of early meiotic prophase I [6, 24, 37–43]. Some authors doubt and even reject this [50]. They argue that the univalent chromosomes in premeiotic haploid nuclei of Zygomycetes already possess axial chromosomal elements characteristic of meiotic leptotene, and sometimes they form the SC via chromosome foldback [51]. However, these doubts are easily dispelled since it is known that the program of meiosis already starts in the haploid premeiotic nuclei of Ascomycetes [6, 33]. Moreover, it is known that synthesis of proteins of axial cores in yeast and mammals and their self-assembly begin as early as in premeiotic interphase [52].

In mammals, the axial chromosome core that at pachytene becomes the lateral SC elements contains two major meiotic proteins, SCP2 and SCP3 [42]. However, these proteins are last to attach to the axial core appearing during premeiotic interphase. The assemblage of the meiotic chromosome axial cores and later the SC occurs as follows. At premeiotic interphase, the early axial chromosome core contains only the Rec8 protein; next, it incorporates SMC (structural maintenance of chromosomes) proteins [52]. By the onset of the zygotene stage, the axial cores incorporate proteins SCP2 and SCP3. This completes the axial core assembly and launches chromosome synapsis and forming of the SC proper. The chromosome axial cores are gradually joined pairwise by means of the SCP1 protein, which is inserted between them in the form of submicroscopic filaments. In the mature SC at pachytene, the paired axial cores are referred to as the SC lateral elements (Figs. 3b, 3c; Fig. 4). The transverse protein filaments act as "half-bridges" between the lateral SC elements playing the role of "zipper teeth." The C end of the SCP1 protein is joined to the lateral SC element while the N end joins to the subterminal region of the N end of the SCP1 protein in opposite orientation, which forms the "counter tooth" of the "zipper" (Fig. 4). The half-bridge "teeth" are located periodically along the total length of the central space between the lateral SC elements. The two globular N ends joined in the central SC space form a bulge. Under an electron microscope a series of these bulges located along the axis of the central SC space looks like a third line—the central SC element—between the two lateral elements (Figs. 3b, 4). Speaking figuratively, the zipper fastening was "invented" by nature in the epoch of the appearance of meiosis in unicellular organisms.

In yeast *S. cerevisiae* the SC consists of proteins lacking the primary structure homology with the proteins of the mammalian SC but has essentially the same structure [46]. A more detailed description of the SC proteins is given in reviews [53, 54].

The elementary chromatin fibrils consisting of DNA, histones, and other chromosome proteins are attached to the lateral SC elements. In terms of SC ultrastructure these fibrils are referred to as lateral chromatin loops. This terminology is convenient for the narrow purpose of describing the SC morphologically but poorly suits cytogenetics since these lateral loops are none other than chromatids of homologous chromosomes that are in fact along the SC in the form of loop-like serpentine of continuous chromatin fibrils. Thus, homologous chromosomes adjoin the lateral SC elements from two sides, and this "point contact" occurs in spots of the loop attachment to the lateral SC elements along the total SC length.

Figure 3d presents an electron-microscope photograph of an ultrathin section of a murine spermatocyte nucleus showing an SC with lateral chromatin loops.

The discovery of the SC and the establishment of its presence in meiosis in the overwhelming majority of multicellular eukaryotes were a significant advance of researchers of meiosis in the late 20th century. Another important discovery concerning the ultrastructural organization of meiosis and general organization of chromosomes consisted in the fact that meiotic chromosomes of all animals are present in the "lampbrush" form not only in oogenesis (at meiotic diplotene) but also in spermatogenesis (at meiotic pachytene) (Fig. 3d) [55]. In plants the same principle is probably observed but since their lateral chromatin loops are long and rumpled they do

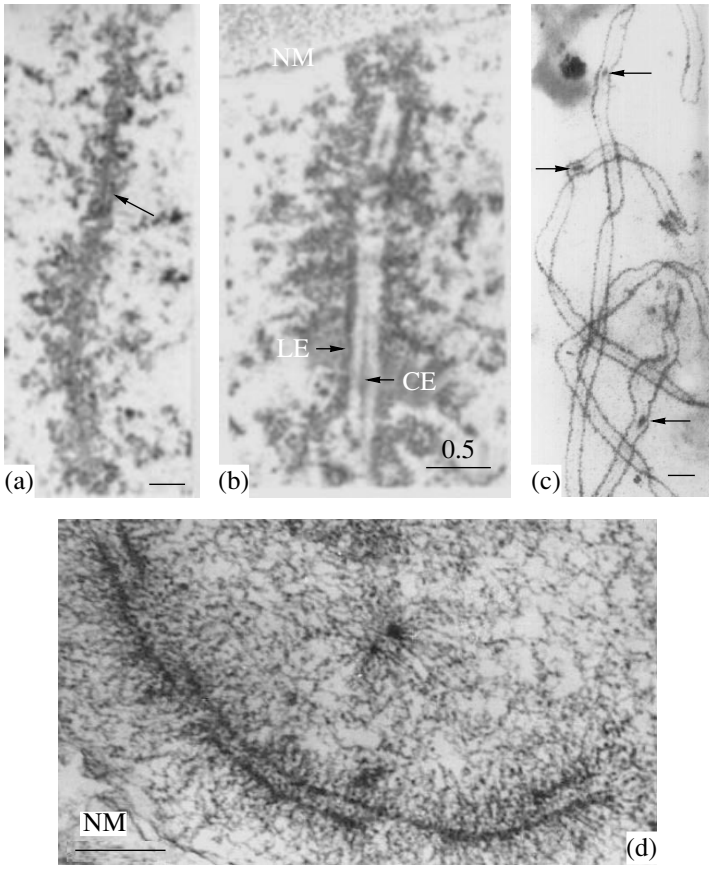

Fig. 3. Electron microscopic picture of chromosomes and synaptonemal complexes in meiotic prophase I of plants and animals. (a) A chromosome fragment of lily *Lilium candidum* at the leptotene stage of meiosis; the chromosome axial core is shown by an arrow; ultrathin section. (b) A fragment of a bivalent with the synaptonemal complex (SC) in lily at the zygotene stage of meiosis; ultrathin section. LE, lateral SC element; CE, central SC element; NM, nucear membrane. (c) A fragment of a nucleus of a rye microsporocyte destroyed by a hypotonic shock and spread on a slide. SCs depleted of chromatin can be seen; recombination nodules are shown by arrows. (d) A fragment of a nucleus of a mouse spermatocyte with the SC; untrathin section. Scale bars: 0.5 μm.

not form neat lampbrush structures characteristic for chromosomes of amphibians and birds (Fig. 3b). However, this last assumption needs to be proved.

The association between chromatin and the SC is graphically illustrated in the universal model of the chromosome structure developed by Stack and Anderson [43].

The Evolutionary Mystery of Proteins of the Synaptonemal Complex

The primary structures of the SCP1 protein in mouse, rat, Chinese hamster, and human are 74 to 93% homologous. The rat SCP2 protein is homologous to the corresponding human protein by 63%. The proteins of both types exhibit nearly 100% homology of individual domains [54]. This is not surprising because in terms of evolution rodents and primates have diverged relatively recently.

The yeast SC proteins of an analogous function lack sequence homology with the corresponding mammalian proteins. This is also understandable if we consider only morphology of the SCs since the evolutionary distance between mammals and Ascomycetes is great. Given that the SCs in these and other distant taxa have common general pattern of organization, their absolute sizes (e.g., width), fine structure of the central SC space, and ultrastructure of its lateral elements are specific for orders and classes but considerably differ between taxonomic types. For instance, in yeast and nematodes the width of the central SC space is 70–100 nm, and the width of the lateral elements is about 15 nm. In birds the corresponding parameters are 150 and 25 nm [39, 41]. These figures serve as the upper and lower limits of the transverse SC measurements in all eukaryotes. The SC size in insects and mammals correspond to the middle zone of this interval. In insects, the central space has a latticed structure whereas in higher plants and mammals it is amorphous. The lateral SC elements of three species of *Ascobolus* fungi display species-specific banding; their proteins are probably also species-specific ([51]; see also [40]). Collectively, these data

indicate that the species-specific ultrastructure of SC is neutral in context of macroevolution.

Another thing about SC proteins is surprising, and I have already discussed an analogous instance with regard to kinetochore proteins. It is surprising that in evolutionarily distant taxa structurally nonhomologous proteins are used to assemble SCs that have the same structure and function. We can draw an analogy between the principle of the SC formation in different organisms and the construction of houses of different sizes, from different materials and for different climates but designed according to one principle (i.e., having walls, roof, and windows) and sharing the function of sheltering their inhabitants. In the same fashion, the SC serves as a shelter for recombining chromosome sites. Importantly, the SC must align parallel homologous chromosomes, maintain some space between them (the central SC space) so as they could recombine, and kept these conditions as long as required to complete recombination and chiasma formation.

Interestingly, the SC assembly in evolutionarily distant organisms, such as yeast *S. cerevisiae* and mammals, involves "standardized" construction elements. For instance, the transverse filaments ("beams") connecting the SC lateral elements ("walls" of the "house") have the same construction. They consist of rather simple proteins (Zip1 in yeast and SCP1 in mammals) belonging to the class of intermediary proteins. Each of these proteins contains three polypeptide domains, the central of which is rod-shaped due to a long coiled coil. The length of this rod-shaped domain and the distance between the lateral SC elements are strongly correlated. This rule holds not only for wild-type organisms but also for a series of yeast mutants with deletions within the rod-shaped domain ($r = 0.97$, $P < 0.001$) [56, 57]. This high and statistically significant correlation indicates a causal relationship between the length of the central domain of these proteins and the distance between the lateral SC elements. A similarity of molecular organization of the SC transverse filament protein Zip1 in yeast and the SCP1 protein in mammals together with the above correlation suggest that these principles extend to organisms from other taxa, in which the length of the SC transverse filaments coincides with that in yeast and mammals. Using this analogy, it was shown that gene *c(3)G* of *D. melanogaster* controlling the SC assembly is the gene whose protein product forms the transverse SC filaments. The positive result of a computer-aided screening for the primary structure of this gene and its product [57] coincided with the result of an experimental search of the *c(3)G* nucleotide sequence and its protein by means of molecular cytogenetic methods [58].

Recombination Nodules As Compartments for Recombination Enzymes

At zygotene and pachytene, the central space of each SC contains the co-called recombination nodules (RNs) (Fig. 3b). The number of "early" nodules at late zygotene is 4 to 10 times higher than the number of "late" nodules at late pachytene [6, 43]. It was shown that the RN number at late pachytene corresponds to the chiasma number in various organisms [6, 43, 59].

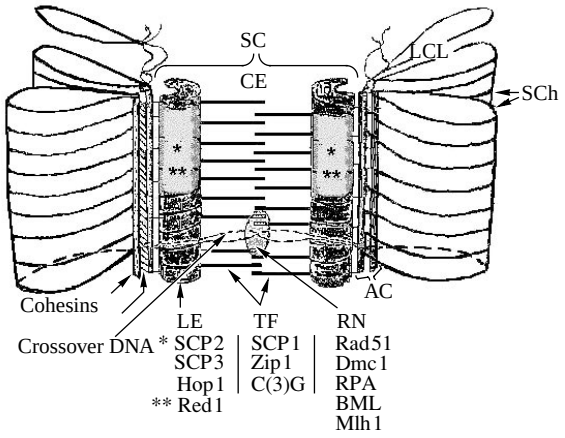

Fig. 4. Hypothetical scheme of the synaptonemal complex (SC) structure in budding yeast, *Drosophila*, and mammals. LCL, lateral chromatin loops; SCh, sister chromatids; CE, central SC element; LE, lateral SC element; TF, transverse filaments between two LEs ("teeths" of the zipper); RN, recombination nodule; AC, chromosome axial cores contained in lateral SC elements; SCP1, SCP2, SCP3, proteins forming structural SC elements in mammals; Hop1, Red1, Zip1, their functional counterparts in yeast; C(3)G, a functionally analogous protein product of gene *C(3)G* (otherwise referred to as gene *CG17604*); Rad51, Dmc1, Mlh1, RPA, BML, enzymes participating in recombination and production of crossover DNA molecules in yeast, *Drosophila*, and mammals, which were experimentally detected in recombination nodules.

RNs consist of DNA and proteins. Using immunocytochemical methods, RNs were shown to contain enzymes required for recombination of DNA molecules. Studies of different authors conducted for the last 25 years on various model organisms (fungi, plants, and animals) demonstrated that chiasmata are formed precisely at the chromosome loci where recombination nodules are located (see [6, 43]). Recombination nodules serve as ultrastructural compartments of recombination enzymes, or, returning to our analogy, "kitchen space" within the "house," i.e., the SC (Fig. 4). Several "processors" ("kitchen robots")—recombination (conversion and crossing over) enzymes—successively operate in RNs [60–62]. Interestingly, due to a reduction in the width of the SC central space in *S. cerevisiae* mutants, which was caused by the aforementioned deletions within the central domain of the transverse filament protein Zip1, the construction of the "house," the "kitchen" of which is the place for recombination, is deteriorated to such an extent that the crossover frequency substantially drops. This means that the operation of "robots" in a small "room" or in a tumbledown "house" is ineffective (Fig. 5).

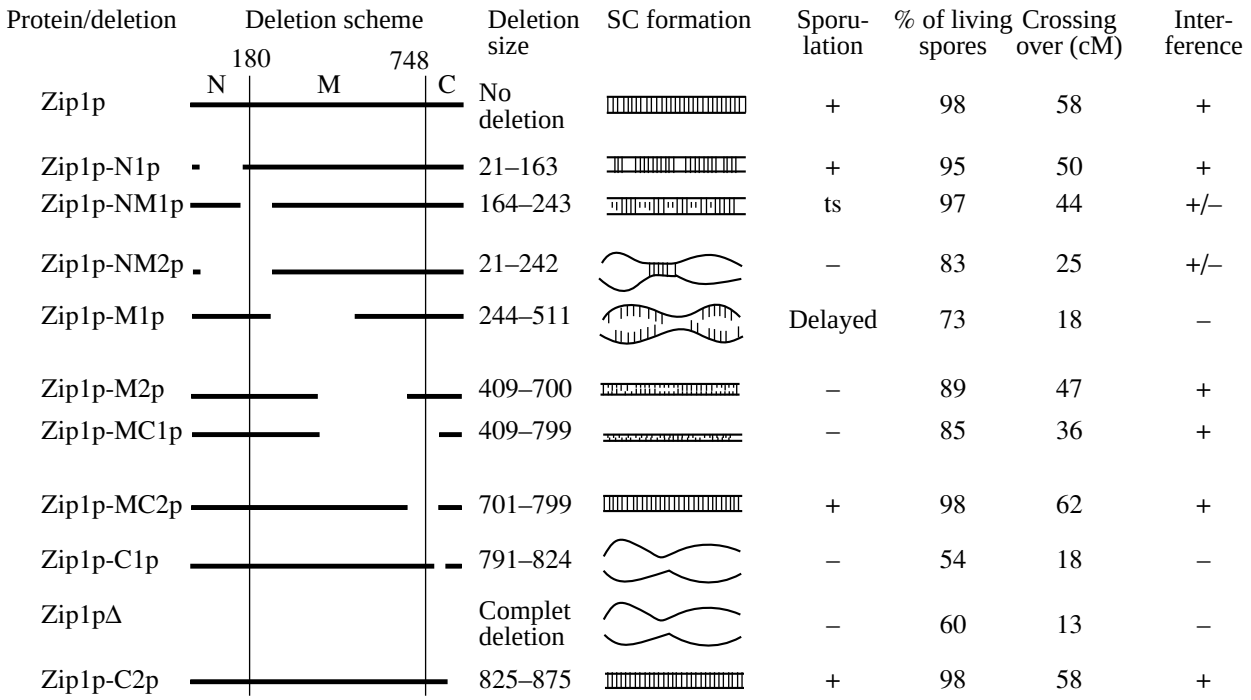

Fig. 5. Scheme of experimental deletions in molecules of protein Zip1 of *Saccharomyces cerevisiae* leading to the alterations in synaptonemal complex morphology indicated in the column "SC formation." N, M, C, structural domains of the protein (M, central domain; N and C, terminal domains). Positions of amino-acid residues in the protein and intervals covered by the deletion are indicated by digits. The column "Sporulation" shows the deletion effect on sporulation (+ sporulation; – no sporulation; ts, temperature-dependent sporulation). Other colums present the deletion effect on the number of living spores (in %), on crossing over (in cantimorgans, cM), and on crossover interference (after [44] with modifications).

Some of recombination enzymes are borrowed by meiotic cells from somatic ones, which use the molecular mechanism of recombination to repair double-strand DNA breaks while other of these enzymes are specific for meiosis. Meiosis-specific enzymes serve to increase the efficiency of meiotic recombination. Figure 6 shows the progression of DNA recombination as the SC forms and functions and the operation of some recombination enzymes during meiotic prophase I. In contrast to evolutionarily neutral SC proteins, recombination enzymes exhibit striking homology even between members of different kingdoms. The key recombination enzymes, protein Rad51, is a RecA-like protein inherited by eukaryotes from bacteria. For instance, bacterium *Escherichia coli* has RecA protein. Thus, eukaryotes inherited the molecular mechanism of recombination from prokaryotes.

Yeast protein Rad51 operates as a heterodimer with protein Dmc1 [60]. In the nematode *Caenorhabditis elegans*, the genes were fused producing one protein [63]. This is an example of protein evolution by shuffling their structural domains (see [56]).

In *S. cerevisiae*, antibodies against the Rad51 protein have a common epitope with the Rad51 protein of higher plants, and Rad51 of tomatoes is homologous to its counterpart in rye (see [4]), which confirm their great evolutionary age and conservatism of the molecular mechanism of recombination.

THE APPEARANCE AND EVOLUTION OF MEIOSIS

The Role of Crossing Over in Evolutionary Formation of Meiosis

The ancient meiosis was probably formed on the basis of mitosis [50, 64, 65], likely because of an appearance of new (or somewhat altered) genes. These could be genes of kinetochore "nondisjunction" (maybe mutated genes for regulation of cohesin cleavage) and SC genes appearing de novo. These evolutionarily younger genes were needed in meiosis for fixing together the centromeric regions of two sister chromatids of one chromosome (e.g., gene *SPO13* of *S. cerevisiae* and gene *meiS322* of *D. melanogaster*, see above) and chromosome arms (gene *ord* of *D. melanogaster* and genes of the SC proteins), and, of course, these were genes for effective meiotic recombination.

The SC fragments are preserved in the chiasma zone at metaphase I, after the disappearance of the SC lateral elements in 99.9% of the other chromosome loci. At meiotic diplotene, when only the residual SC fragments are visible in the nucleus, it is within these fragments that recombination nodules are observed ([59, 66], see

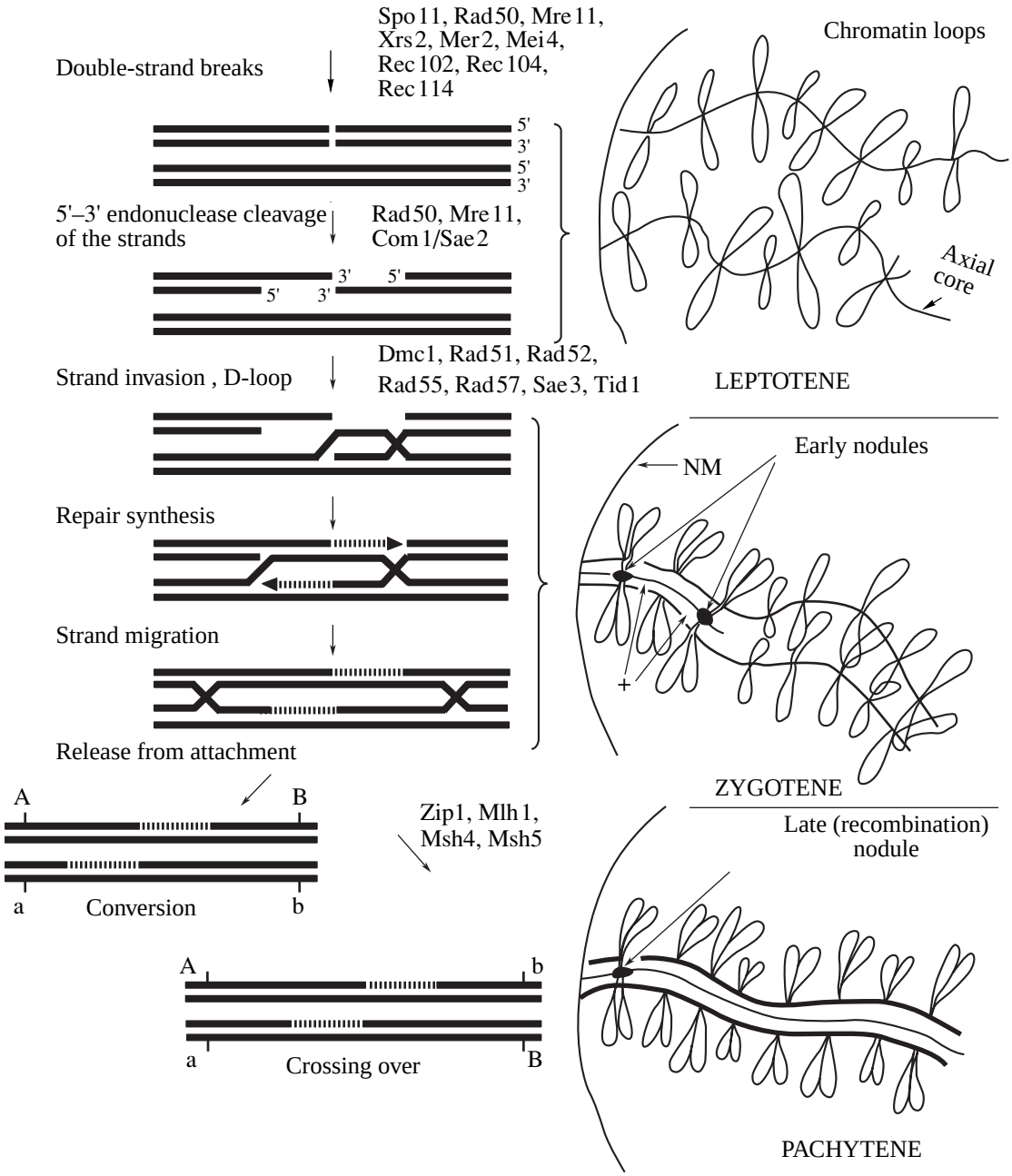

Fig. 6. Schematic comparison of the stages of DNA recombination with the stages of formation and functioning of synaptonemal complexes. Designations of recombination enzymes, stages of meiotic prophase I, and morphological structures of chromosomes and the synaptonemal complex are indicated. The forming central element of the synaptonemal complex is indicated by +. NM, nuclear membrane.

[6] for review). Thus, the SC appearance was a systemic mutation (in Goldschmidt's sense) at the cell level, which permitted creation of meiosis in its current "classical" form. The same is probably true for the role of chiasmata and sister-chromatid nondisjunction in the cell division that due to them became the first of the two meiotic divisions. I would like to remind here the above remark that the absence of DNA replication prior to the second meiotic division is only a consequence of the kinetochore nondisjunction in the first division.

The appearance of this complex of traits transferred unicellular organisms to the pathway of arogenesis [11–14], i.e., directed them to the new, more progressive level of morphophysiological development.

One might say that meiosis became an aromorphosis of unicellular organisms since it resulted in the formation of progressive and evolutionarily advanced mechanism of reduction of the chromosome number and in the possibility of alteration of the diploid and

haploid phases of development. Diploidy as an error-proof feature was fixed in evolution.

The role of crossing over in the evolution of classical meiosis lies primarily in the fact that it promoted the appearance of chiasmata and classical meiosis in the progressive evolution of unicellular organisms rather than in the enhancement of combinatorial ability of chromosomes. In other words, the biological role of crossing over is essentially the creation and maintenance of the most advanced known meiotic mechanisms for reducing the chromosome number during the first phase of reproductive process (gametogenesis, sporogenesis) in eukaryotes. Only accepting that the mechanism of crossing over and resulting chiasmata were advantageous for creating a fundamental and biologically significant phenomenon of chromosome number reduction, we can realize that the role of crossing over in evolution (i.e., enhancement of combinatorial ability of genes) is clearly secondary. Geneticists erroneously accept the latter role of crossing over as the most important, which is reflected in many monographs and textbooks, including good ones (e.g., [67]). Murray and Szostak [29] suggested that the primary role of crossing over consisted in creation meiosis itself although this idea could have been advanced before them. I fully share this view.

In her theoretical paper, Maguire [68] examined evolutionary significance of recombination based solely on combination of independently segregating chromosomes. First of all, Maguire confirmed the view that recombination creates advantage in adaptation of populations for changing environments upon selection for an optimal phenotype. Then she compared two types of recombination and, following Crow [69] and Maynard Smith [70], states that combinations of independently inherited genes (linkage groups) can sometimes be of more significance than gene combinations arising via crossing over within linkage groups. For instance, combinations of independently inherited genes is more important for an organism that have more than two pairs of chromosomes [69, 71]. Furthermore, in one of the sexes of some organisms (for example, in *Drosophila* males) crossing over was eliminated in evolution; apparently, even fewer eukaryotic organisms have only two chromosome pairs. Organisms with one or two pairs of chromosomes (e.g., *Ascaris megalocephala*, *Haplopappus gracilis*) probably have crossing over, which must play for them a more important role than independent segregation of the maternal and paternal chromosomes of each pair. Citing Maguire [68], "it has also been calculated that the advantage of genetic segregation (apart from recombination) in a sexually reproducing diploid organism may offset the twofold reproductive advantage of asexual reproduction (Kirkpatrick and Jenkins, 1989). In the presence of such segregation, a single advantageous mutation may readily become homozygous. Although there are many asexual species of eukaryotes, generally the relationships of these to sexually reproducing forms suggests that they have evolved relatively recently from sexually reproducing ancestors." Thus, the view that the role of crossing over and chiasmata in reducing the chromosome number was primary for the establishment of meiosis and the advantages of crossing over as the factor of recombination of linked genes was a consequence and a secondary factor in this scenario is not unusual. This view can only seem unusual for the evolutionists who are not familiar with the cytological mechanism of meiosis.

It was proposed that meiosis appeared on the basis of crossing over. Supposedly, crossing over was first used for repairing DNA breaks, which had accumulated in cells prior to the onset of meiosis [72]. This is only partly true. The molecular mechanisms of crossing over are indeed used to repair double DNA breaks (DSBs). However, first, contrary to the view of Gershenzon [72], this repair takes place also in somatic cells [73, 74] and cells do not have to "wait" for meiosis to start repair, and, second, at premeiotic interphase and meiotic leptotene, new double-strand DNA breaks massively occur due to operation of meiotic endonucleases. These breaks are immediately used at the next meiotic stage, zygotene, as sites of recombination (crossing over). Thus, we cannot regard DNA repair as the key function of meiosis and reproduction. Instead, we may assume that the molecular mechanism of DSB repair was employed by archaic unicellular eukaryotes as a basis for gradually changing "simply DNA repair" into a process of chromosome number reduction. However, as noted above, the "invention" of chiasmata also involved the mechanism of maintaining local sister-chromatid cohesion in the vicinity of chiasmata, and the creation of the complete "set" of meiotic "tools" required also a mechanism for nondisjunction of sister kinetochores.

Relict Mechanisms of Meiosis

The homology of major meiotic traits in various eukaryotic taxa is shown in the table. This homology is indeed striking as are the well-known exceptions from the classical scheme of meiosis also listed in the table.

Exception 1. Some lower Protozoa have one-step meiosis, i.e., meiosis consisting of one cell division [64, 65]. It is possible that in this type of meiosis, the kinetochore lacks disjunction at early anaphase and the disjunction occurs during anaphase which is accompanied by a cascade process of separation, first of homologs, and then, during the operation of the division spindle, of sister chromatids of each homologs (or vice versa, which is of no importance here).

Exception 2. This is meiosis without SC in fungi *S. pombe* and *A. nidulans*. At meiotic prophase I in *S. pombe* protein linear chromosome elements are formed. These elements are analogous to the axial chromosome cores formed at prophase I in organisms having SC (e.g., *S. cerevisiae*). However, these linear elements do not transform into the lateral SC elements.

Cytological traits of meiosis

Kingdom	Taxa	Meiotic division I			Meiotic division II
		bouquet and other chromosome clusters	synaptonemal complex	crossing over and (or) chiasmata	
Protists	**Sporozoa**	?	–	?	+
	Grebnickiella gracilis	?	–/+	?	+
	Foraminifera	+	+	+	+
	Infusoria	+	+	+	+
Fungi	**Fungi imperfecti**				
	Aspergillus nidulans	?	–	+	+
	Ascomycetes				
	Schizosaccharomyces pombe	+*	–	+	+
	Saccharomyces cerevisiae	+	+	+	+
	Basidiomycetes	+	+	+	+
Multicellular animals	**Cnidaria**	+	?	+	+
	Nemathelmintes Nematoda	+	+	+	+
	Arthropoda				
	Insecta				
	Lepidoptera				
	Bombyx mori				
	♀	+	+**	–	+
	♂	+	+	+	+
	Diptera				
	Drosophila melanogaster				
	♀	+***	+	+	+
	♂	?	–	–	+
	Orthoptera	+	+	+	+
	Chordata	+	+	+	+
Plants	**Gymnospermae**	+	+	+	+
	Angiospermae	+	+	+	+

Note: The presence (+) and absence (–) of the traits is indicated. The cases of the presence of the trait not described in literature or not known to the author are shown by question marks (?). Asterisks (*) indicate departures from the classical meiosis morphology: * *Schizosaccharomyces pombe* lacks the chromosome bouquet in early prophase I; its role in bringing chromosomes together is fulfilled by the horse-tail configuration; ** *Bombyx mori* females have the SCs but after pachytene they transform into massive protein bodies preventing crossing over of homologs; *** *Drosophila* females lack the chromosome bouquet but their centromeres in early prophase I are arranged into a chromocenter.

This means that *S. pombe* lacks a protein analogous to Zip1, which could provide a zipper between the linear chromosome elements. In *S. pombe* the apposition and alignment of all chromosomes (including homologous ones) within the prophase nucleus is effected via chromosomes forming a configuration referred to as a horse tail. A short-term homologous chromosome pairing takes place prior to and during meiotic metaphase I, i.e., this principle of homologous pairing and separation formally corresponds to the touch-and-go principle of meiosis in *Drosophila* males (see below). In *S. pombe*, recombination nodules are present. However, they are not fixed within the SC (which is absent) but are located on chromosomes and separated by unrestricted distances. Consequently, this yeast species lacks crossover interference while crossing over per genetic map unit occurs more frequently than in *S. cerevisiae*.

Exception 3. This is meiosis in males of *Drosophila* (and some other members of Diptera and Coleoptera) that involves chromosome number reduction but no SC, crossing over, and chiasmata. In this case, at meiotic metaphase I in males, homologous chromosomes for a short time are linked by protein filaments termed collachores [75, 76]. At the first glance, the most striking feature of this type of meiosis is that it is underlain by different mechanisms in males and females of the same species. We have described the genetic control of these mechanisms elsewhere [5, 21, 77]. In brief, acciden-

tally and unfortunately for *Drosophila* flies, some genes responsible for the SC formation turned out to be located on the X chromosome. *Drosophila* males have sex chromosomes XY and, by contrast to humans, even X0. In any case, they have a twofold lower dose of the key SC gene(s) located on the X chromosome. Numerous experiments conducted by different research teams showed that exactly the dose of these genes determined the possibility of the SC formation (see [21, 77]). Moreover, an X-chromosome segment was found, a deletion or duplication in which leads to a change of sex in *Drosophila* and to the gain of loss of the capability to form the SC [21, 77]. In other words, in *Drosophila* not only sex but also the SC presence or absence are determined by the balance of the number of X-chromosome segments carrying the key gene. As a result, *Drosophila* males had to employ the more evolutionarily old mechanism of chromosome number reduction, i.e., touch-and-go (see above), which is also characteristic of yeast *S. pombe*. Hence, evolution (at least, in flies) did not lead to a loss of the archaic program of meiosis. In females, this ancient program stayed unclaimed, and in males, it was used for meiotic reduction of chromosome number at the absence of a gene dose sufficient to form the SC.

As seen from the list of organisms (*A. nidulans, S. pombe, D. melanogaster*, and other dipterans) possessing the achiasmatic mode of chromosome pairing touch-and-go, this mode is relatively widely spread in nature. It may be inherited from ancient unicellular eukaryotic organisms, of which this mechanism of homologous chromosome separation was characteristic. The possibility that it evolved as an alternative to the classical meiosis scheme is less plausible. In any case it presents an exception to this scheme.

The existence of sex-specific meiosis mechanisms in *Drosophila* indirectly corroborates the validity of the above considerations with regard to the biological role of crossing over. Having lost half of possibilities for crossing over, i.e., lacking crossing over in males, drosophilids did not start evolving at a lower rate than other eukaryotes; conversely, their evolution is rapid (see [13]). Importantly, they retained meiosis despite of the fact that one sex had to use an archaic mechanism of chromosome number reduction preserved in the depth of the genome.

The ability of the genome to preserve by-pass regulation pathways for vital cellular processes is illustrated by other examples related to meiosis. For instance, mutants of yeast *S. cerevisiae* have several metabolic by-passes to preserve recombination in the case when certain recombination enzymes cannot perform because of mutations of the encoding genes (see [2]).

Thus, the set of traits characteristic of classical meiosis has evolved gradually. It was established as early as in the epoch of unicellular eukaryotes similar to the modern higher Protozoa and unicellular fungi, such as *S. cerevisiae*.

The appearance of a set of traits new for ancient unicellular organisms, i.e., kinetochore nondisjunction, formation of synaptonemal complexes and classical chiasmata, and the use of this set in the reproductive process was an event equal to a new aromorphosis of ancient eukaryotes. These alterations in the cytological mechanisms underlying meiosis arose via a multi-step mutational changes of cellular structures. They resulted in new progressive adaptation of diploid unicellular organisms that combined dosed variation with sufficient genome conservatism and phenotype stability. Haploidizating cell division was transformed into the classical meiosis because of the synaptonemal complex, chiasmata, and centromere nondisjunction in the first meiotic division.

Here, I would like to make an important comment. Application of terms like aromorphosis and other terms borrowed from comparative morphology of multicellular animals [78] to intracellular structures may appear very arbitrary. I dared to take this step to stimulate a discussion rather than to affirm my own assumptions. The evolution of unicellular organisms is significant for the general theory of evolution, and its description requires standard terminology. To this end, it is expedient to use the available terms (as was done earlier) [79] rather than to introduce new ones. Terms aromorphosis, idioadaptation, and cenogenesis were coined by Severtsov [78] to denote morphophysiological changes leading to progressive evolution. Severtsov considered, among others, changes in the structure of cells; for example, those of smooth muscles in the worms–reptiles–mammals series. To describe progressive changes in this series, he used the term aromorphosis.

In this context, the differences in meiosis between *Drosophila* males and females can be described as idioadaptation, i.e., a process of adaptation of members of a particular taxon to certain environments, and in our case, to the genotypic background of the organism (see above text on the localization of the SC genes on the X chromosome). As in the examples of idioadaptations considered by Severtsov [78], in *Drosophila* males chromosome pairing has reversed to the archaic touch-and-go type, which played the role of a progressive adaptation in the evolution of these insects.

Putative Stages of the Evolution of Meiosis

In their monograph rich in factual material and thought, Seravin and Gudkov [50] describe at least four types of somatic reduction of the chromosome number in modern protists that have agamous reproduction. These types are as follows: (1) fragmentation of the nucleus, (2) multipolar mitosis, (3) deploiploidizing mitoses, and (4) parameiosis. Pondering on the evolutionary pathways of meiosis, the authors focus their attention on the two latter types. In their view, “depolyploidizing mitoses, when they are accompanied by chromosome conjugation and crossing over, in essence are not different from meiosis; some authors regard

them as meiosis .of vegetative cells" [50]. At parameiosis, "event characteristic of meiosis (chromosome conjugation, crossing over, haploidization) occur in a successive series of daughter nuclei." And further: "There are grounds to believe that in the process of evolution, under natural selection, all these components may have been joined in one nucleus, which would have inevitably give rise to true meiosis. If this assumption is true, meiosis could have evolved by different pathways in different protists" [50]. Note that this primarily concerns the events of the pasts having occurred in the ancestors of the modern protists that currently exhibit depolyploidization and parameiosis. However, the evolution of the modern protists may continue. The ongoing microevolution in modern bacteria is apparently beyond doubt, and there are grounds to suppose it for protists.

I mainly share the rather cautious conclusions on the possible causes and sequence of events in the evolution of meiosis reached by the authors of this interesting publication [50]. My view is based on the concepts that gained a foothold in the scientific literature during the past decade. These concepts are, in particular, based on the results of discussions at the international conferences, which are mentioned at the beginning of this paper (see [4]). Some recently established key facts and new general conclusions collectively drawn at these conferences are considered in the present review.

I would like to focus on the conclusions of Maguire, the thoughtful and skillful author who studied meiosis [68]. She reasonably believes that meiosis is too complex to have arisen at once and proposes a stepwise model for its evolution. (1) The first step might be the development of a "tentative" haploidization by means of a rapid series of mitotic nondisjunctions occurring under conditions where haploidy is favored. This haploidization may have resulted from conditional (e.g., temperature-sensitive) mutations which caused sister centromere cohesiveness in the past mitotic metaphase. (2) Next probably a rudimentary synaptonemal complex type structure was formed. This structure could first appear between chromosomes at the sites where recombining homologous chromosomes form Holliday junctions. Later these configurations extended along chromosome pairs (bivalents). Although the production and maintenance of these structures was costly to the cell, they have directly served a new function—haploidization—by setting the stage for the production of haploidy in one division, under conditions where it was evolutionarily advantageous. (3) The second acquired functions of the synaptonemal complex (or associated archaic structures) was a promotion of an increased crossover frequency. This may have partly happen by increasing the frequency of the isomerization-type reaction (see Fig. 6). The resulting recombination of linked genes could have been advantageous under some conditions. (4) Finally, it was proposed that the capability was acquired for enhanced association of sister chromatids during the period between pachytene and anaphase I to give rise to chiasma "construction" and chiasma-mediated disjunction. Thus, the relatively costly synaptonemal complex maintenance until anaphase I became could be abandoned without losing the reductional disjunctive capability of the homologs.

This scheme needs some commentaries.

(1) The view on a stepwise appearance of meiosis has been directly or indirectly stated by many authors (e.g., [50, 64 65]). Moreover, it was repeatedly suggested that meiosis is very likely to originate polyphiletically in various branches of the evolutionary tree of uni- and multicellular organisms ([50, 64, 65, 70] and other references). I think that this view is favored by, for example, the fact that various discrete elements and groups of the cytological events of the classical meiosis are currently observed in unicellular organisms that reproduce asexually or via pseudomeiosis as well as in organisms that exhibit nonclassical mitosis and somatic chromosome reduction (see [50]). These rather diverse modes of cell division require systematization and revision by means of modern tools of cell biology. However, even as they are they present invaluable material for thought and putative evolutionary constructions.

(2) The rudimentary, or archaic, SC mentioned by Maguire (see above) is formed in protists only in the centromeric region. This SC was found in *Grebnickiella gracilis*, which have one-step meiosis [80]. The SC is very small in length (0.16–0.18 μm) and forms only in one region of each bivalent, namely, between the kinetochores of homologous chromosomes. Kinetochores can be easily identified under an electron microscope because of their characteristic three-layer structure. They serve as the SC lateral elements, while the central SC element appears between them. Molon-Noblot and Desportes [80], and later Raikov [81] suggested that in these unicellular organisms homologous pairing is produced only by these short segments of the rudimentary SC. One can speculate that for the appearance of this SC, "only" one protein of the yeast Zip1 type may have been needed to form the zipper structure (the transverse SC filaments). The lateral element proteins were not required at that stage: their role in the rudimentary SC was played by kinetochore proteins. Hence, only one advantageous mutation was required to give rise to the rudimentary SC. This, for instance, could be a mutation causing shuffling of protein domains of an intermediary (e.g., cytoskeleton) protein. This rudimentary SC consisting of kinetochores and transverse elements can function only in very small chromosomes like those of *Grebnickiella gracilis.* Larger (containing more DNA) chromosomes of other protists require long lateral SC elements.

(3) At this point, the reasoning of Maguire appear dubious and somewhat contradicts the aforementioned Maynard Smith's hypothesis [70] on the role of crossing over in the evolution of classical meiosis. The SC presence decreases the total crossover frequency due to crossover interference (see above). It is known that one

chiasma per bivalent is sufficient for successful segregation of homologs in meiosis I (see, e.g., [6, 43]). Classical meiosis of *S. cerevisiae* is more advanced than meiosis of *S. pombe* and *A. nidulans* due precisely to the low crossover frequency per unit length of DNA molecules.

(4) The archaic mechanism of preserving the SC in the cell until the onset of anaphase I mentioned by Maguire in fact exists in some modern butterflies, e.g. in females of silkworm *Bombyx mori*. The explanation of this is clear although some authors are perplexed by this example. The point is that in *Bombix mori* females the central SC space at pachytene is filled with homogeneous protein material [82] so that crossing over and chiasma formation are impossible. The same homogeneous material seems to prevent the programmed proteolysis of cohesins and SC proteins, and the modified SC persists until anaphase I. Based exactly on this example Maguire proposed that achiasmatic meiosis with the SC persisting until anaphase I was a precursor of the modern meiosis. I am also inclined to think that this is an instance of preserving the archaic type of meiosis in one of the sexes of a modern bisexual insect. In this case, this archaic trait must be nevertheless less old than the mechanism of achiasmatic pairing and touch-and-go chromosome segregation in yeast *S. pombe* and males of *D. melanogaster.*

Consider the last example. It is discussed in [50]. In a highly polyploid radiolarien *Aulocanta scolyantha*, the chromosome number reaches 2000. This organism produce spores with the chromosome number of eight. The spore formation is preceded by depolyploidization occurring via several cell divisions. One of them involves the appearance of typical SCs and bivalents [83, 84]. After the stage of the marked expression of the SC, the axial cores of chromosomes (i.e., lateral elements of the degraded SC) are preserved until metaphase. These are traits of a typical meiotic prophase I. In diploid unicellular organisms whose cytological examination under a light microscope is problematic (e.g., *S. cerevisiae*), these traits are regarded as reliable markers of prophase I of meiosis. In particlular, the SC serves as a marker of pachytene [33]. However, the authors that have studied depolyploidization in *A. scolyantha* [83, 84] are reluctant to refer to the division involving the SC formation as to meiosis. These authors did not succeed to score the number of SC in the cells. Their study did not clarify how the chromosome number in these cells is reduced from about 2000 to 8. This raises a number of questions. For instance, what is depolyploidization: a series of reduction divisions lacking the features of classical meiosis? On the other hand, it may well be that the "high ploidy" of this organism is an artifact. Before the SC formation, the chromosomes may attach by their ends becoming, so to say, polymeric, and the diploid chromosome set would thus be reduced just once. Publications [83, 84] do not clarify these issues. Solving each of such cases requires not only an examination of the number and ultrastructure of the nucleus during the whole cell cycle but also description of these observations in standard terms used for modern description of meiosis.

The above instance of depolyploidization in *A. scolyantha* may be presumably explained differently, e.g., as a series of successive events of chromatin diminution (see [85]). In this case, the multiple cell divisions after the SC formation would be stages of elimination from the cell of "vegetative" ("somatic") chromatin that occur after meiosis involving the SC formation. These rounds of diminution may mimic "depolyploidizing" cell divisions.

Meiosis in unicellular Protozoa and fungi remains the most fascinating field of research as these organisms are the closest current ancestors of the primary prokaryotes, in which the classical type of meiosis had gradually evolved. An intriguing question arises: did meiosis historically appeared after mitosis or did the both division types, meiosis and mitosis, evolved in parallel in primitive diploid organisms? In modern bacteria primitive forms of the achromatic apparatus of cell division were found [85–89]. Further research in this direction, in particular involving extension of the range of examined prokaryotes can yield significant facts for understanding the evolution of meiosis.

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