

## Holocentric Chromosomes

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### Glossary

**Aneuploidy** A change in chromosome number that involves anything other than the entire set of chromosomes (i.e., a change in chromosome number that is not due to polyploidy); most commonly, aneuploidy refers to gains or losses of a single chromosome, a portion of a chromosome arm, or a small subset of chromosomes.

**Agmatoploidy** Increases in chromosome number due to fission. Such changes are common in organisms with holocentric chromosomes (q.v.). Decreases in chromosome number due to fusion are also often referred to as agmatoploid decreases, but these are better referred to using the term symploidy (q.v.). Cf. Aneuploidy, Polyploidy, Symploidy.

**Diffuse centromere** The nonlocalized chromosome structure facilitating spindle fiber attachment in holocentric chromosome mitosis. Most familiar organisms have monocentric chromosomes, which are localized at a particular location of the chromosome. In holocentric chromosomes, the diffuse centromere extends along the entire poleward face of the metaphase chromosome.

**Diffuse kinetochore** Diffuse centromere.

**Holocentric chromosome** A chromosome in which centromeric activity is distributed along the chromosome arms, not localized to a single (occasionally few, more than one) discrete centromeres.

**Holokinetic chromosome** See 'Holocentric chromosome'.

**Postreductional meiosis** Meiosis in which the equational division (in which sister chromatids segregate) precedes the reductional division (in which homologous chromosomes segregate). Cf. Prereductional meiosis.

**Prereductional meiosis** Meiosis in which the reductional division (in which homologous chromosomes segregate) precedes the equational division (in which sister chromatids segregate). Cf. Postreductional meiosis.

**Symploidy** Decreases in chromosome number due to fusion, common in organisms with holocentric chromosomes (q.v.). Cf. Agmatoploidy, Aneuploidy, Polyploidy.

**Polyploidy** A change in chromosome number resulting from duplications of the entire genome, resulting in multiplicative increases in chromosome number (e.g., triploidy or tetraploidy).

### Introduction

Holocentric chromosomes are distinguished by the structure of the kinetochore, which extends along the poleward face of the metaphase chromosome. Because holocentric chromosomes lack a localized centromere, some researchers favor the term holokinetic over holocentric. Holocentric chromosomes are commonly referred to as having a diffuse centromere or kinetochore. Microtubule attachment during mitosis is distributed along the length of the holocentric chromosome, in contrast to monocentric chromosomes, in which the kinetochore and hence microtubule attachment is localized to one region. Thus, chromosomes migrate broadside toward the poles in mitosis. Meiotic holokinetic chromosomes move end-on toward the spindle poles, as the chromosome ends assume the centromeric role. Holocentric chromosome organization has been described for three of the six supergroups in the domain Eukarya (the Eukaryotes): plants (angiosperms, algae, and mosses), animals (numerous arthropod clades, velvet worms, and nematodes), and Rhizaria. The diversity of holocentric groups is particularly striking in the arthropods, including such insect orders as the Lepidoptera (butterflies and moths), Hemiptera (true bugs), Odonata (dragonflies and damselflies), and others; as well as arachnids (spiders and allies) and Chilopoda (centipedes).

Extensive cytological, molecular, and genetic research on the nematode *Caenorhabditis elegans*, in combination with recent work in insects and plants, indicates that holocentric chromosomes

have many structural features and behaviors in common with the more familiar monocentric chromosomes. Studies in *C. elegans* demonstrate that holocentric chromosomes terminate in repetitive sequences similar to those of mammalian telomeres. Studies in the wood-rush *Luzula nivea* confirm this result using a plant telomere repeat and further demonstrate that angiosperm centromere sequences are distributed in several sites on each holocentric chromosome, and that antibodies to kinetochore-associated proteins localize in the same chromosomal sites.

### Mitotic Behavior

Mitotic observations have been important for recognizing holocentricity in many organisms. Holocentric chromosomes lack the primary constriction that was first recognized in 1880 as demarcating the centromere of monocentric chromosomes. The diffuse kinetochore becomes visible at the ultrastructural level in prophase. By metaphase, it is typically a well-differentiated trilaminar structure resembling the kinetochore of monocentric chromosomes. Kinetochore proteins extend longitudinally from isolated loci at interphase to form a continuous, linear body oriented in the outside chromatid grooves at metaphase. At metaphase, the chromosomes align parallel to the equator of the metaphase spindle and lie entirely within the spindle. Microtubule attachments are

distributed along the kinetochore, so that at anaphase the chromosomes move broadside on to the spindle poles.

### Meiotic Behavior

In meiosis, in most organisms that have been examined at the ultrastructural level, no kinetochore structure is seen. Instead, microtubules appear to project directly into the chromatin. At diakinesis of meiotic prophase I, the bivalents of holocentric chromosomes are composed of homologous chromosomes, which appear to be held together in an end-to-end association. In earlier literature, this association was attributed to terminalization of chiasmata, but most evidence now suggests that terminal chiasmata are rare or absent in holocentric chromosomes. It seems more likely that the extreme condensation of the chromatin obscures cytological manifestations of distributed crossovers and gives rise to the apparent end-to-end association of the homologs. Furthermore, proper disjunction of the homologs requires a crossover event, and it appears that the location of the crossover determines which of the two ends of the homologs are associated in the bivalent.

The orientation of the bivalents on the metaphase I spindle varies from species to species. The bivalents may adopt the equatorial orientation and align parallel to the equator of the spindle (equatorial orientation), or they may align parallel to the spindle pole axis (axial orientation). If the bivalent aligns axially, then the sister chromatids segregate to the same pole at anaphase I, so that the first meiotic division is reductional, as occurs in meiosis in species with monocentric chromosomes. This is referred to as prereducational meiosis, and it appears to be the norm for bivalent autosomes in most or all holocentric animal groups investigated. Among plants, postreductional meiosis has been argued to be typically associated with holocentricity based on a long history of meiotic observations. However, this interpretation has been rejected in the animal literature, based on observations in arthropods and nematodes that consistently suggest postreductional meiosis of sex chromosomes and non-bivalent autosomes (e.g., univalents or trivalents), but prereducational meiosis of bivalent autosomes, as well as reinterpretation of the plant meiosis observations.

In *C. elegans* and a wide range of hemipteran species, cytological markers have provided insight into the segregation of axially oriented homologs. Chromosomes align axially at metaphase I and move end on toward the spindle pole at anaphase I. It appears that chiasmata suppress kinetic activity, so that the leading end of each chromosome is the end farthest from any chiasmata. On completion of meiosis I, the sister chromatids remain in association at the ends that were poleward in metaphase I. They align axially with these ends on the equator of the metaphase II spindle, and then at anaphase II, the opposite ends of the chromosomes lead the way toward the spindle poles. Thus, in these organisms, it has been established that both ends of the chromatids adopt 'kinetic activity' in meiosis, with first one end performing this function at meiosis I and the other at meiosis II. Proper orientation of bivalents (metaphase I) and chromatid pairs (metaphase II) appears in *C. elegans* to result from a sheath of microtubule bundles that run parallel to the chromatids. The chromosome end that leads in anaphase is not predetermined by any aspect of

chromosome structure, and polarity typically or always reverses between anaphases I and II.

### Chromosome Rearrangements

It has long been recognized that chromosome fragments and rearrangements that would be lost in monocentric chromosomes may be propagated and become fixed in organisms with holocentric chromosomes. Chromosomes resulting from the fusion of two holocentric chromosomes, for example, may align and segregate to a single spindle pole, whereas in organisms with monocentric chromosomes, the linkage of two chromosomes may result in the formation of dicentric chromosomes that fail to segregate properly. Conversely, fragments from fissions of holocentric chromosomes are retained and may be inherited in a Mendelian fashion, because they retain the capability to attach to the spindle apparatus. In addition to fission (which results in agmatoploid increases in chromosome number) and fusion (which results in symploid decreases in chromosome number), which may be only weakly underdominant or nearly neutral in holocentric chromosomes, holocentric chromosome structure facilitates translocations and inversions. In a recent genome mapping study, the rate of chromosome rearrangements in Lepidoptera was higher than that in nematodes (both holocentric), and nematode chromosome rearrangements were approximately 4 times as rapid as *Drosophila* (monocentric). Yet in spite of the potential genomic chaos that could result from holocentricity, even Lepidoptera exhibits extensive conservation of gene order (synteny) at fine scales.

Comparisons of chromosome variability among organisms with holocentric chromosomes may be biased by sampling intensity, as there has been interest in documenting chromosome variation in the groups that initially show greatest variation. However, even when sampling bias is accounted for, variation in rates of chromosome evolution is dramatic. It is not clear, however, why some holocentric lineages (e.g., *Agrodiaetus* butterflies (in the insect order Lepidoptera, which ranges in diploid chromosome number from  $2n=10-268$ ) and *Carex* sedges of the angiosperm family Cyperaceae, which ranges from  $2n=4-226$ ) exhibit exceptionally high rates of chromosome evolution, while others (e.g., nematodes) appear to have a relatively stable karyotype. Recent study of localized pairing centers in *C. elegans* suggests that in some organisms, the presence of localized chromosome elements may stabilize the karyotype even in the absence of centromeres.

### Evolutionary Implications

In Lepidoptera, phylogenetic comparative evidence suggests that chromosome rearrangements that accrue in allopatry play a role in reinforcing speciation. In the sedge genus *Carex* (Cyperaceae), chromosome rearrangements contribute to genetic diversity within species. These findings suggest that holocentricity is an important determinant of biodiversity patterns in the wide range of lineages in which it occurs. Holocentricity undoubtedly also plays an important role in the evolution of recombination rates. In holocentric chromosomes, the number of chiasmata is very rarely higher than two per homologous

chromosome pair, apparently due to failure of bivalents with more than two chiasmata to segregate normally. Thus chromosome number itself may be the primary determinant of recombination rates, as has been demonstrated in achiasmatic male meiosis in bed bug (Heteroptera) and suggested in *Carex* (Cyperaceae). Beyond effects on recombination rates and genetic and lineage diversification, holocentricity appears to have contributed to the evolution of multiple sex-determining systems in the true bugs (Hemiptera: Heteroptera), where alternative sex chromosome mechanisms have evolved by fission and fusion.

### Outstanding Questions

Our understanding of the behavior of holocentric chromosomes in mitosis and meiosis is based on cytological observations in a wide variety of species, but our understanding of the structure of holocentric chromosomes is based on observations in relatively few species. These observations raise a number of questions regarding the structure and function of the holocentric 'centromere'. For example, how does a holocentric metaphase chromosome become oriented toward only one spindle pole, and how is kinetic activity restricted first to one end and then the other of meiotic chromosomes? Among lineages that have holocentric chromosomes, what are the determinants of the degree of genome and karyotypic stability?

Future molecular, genetic, and evolutionary investigations should provide answers to these questions as they relate specifically to holocentric chromosomes and to the behavior of chromosomes in general.

*See also:* Aneuploidy; Polyploidy.

### Further Reading

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