seem immediately obvious. Biological tissues, even if unpigmented, vary slightly in refractive index, which means that the interfaces between them, and the interface with the water outside, produce slight reflections. This reflected intensity is only a few percent at worst, and in diffuse residual daylight this merges with the background. But in a beam of light from a predator against a dark background, such reflections become visible. In these circumstances the overall reflectance can be halved by darkening the body. The ability to expand chromatophores on a time scale of about a second from dot-like structures to comprehensive body covering is a strategy available to most cephalopods [7], and this is put to good use here to switch from one form of camouflage to a slightly better one.

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Centromere Clustering: Where Synapsis Begins

Centromeres congregate into a large cluster called the chromocenter during *Drosophila* oogenesis. Two recent studies now define a function and a genetic basis for this remarkable structure.

Vijayalakshmi V. Subramanian and Andreas Hochwagen

The formation of haploid sperm and egg cells from diploid germ cells involves some extraordinary chromosome acrobatics. Most of these movements occur in the course of meiosis, a specialized cell division program, during which homologous chromosomes as well as sister chromatids are segregated from each other in successive events. In preparation for the meiotic divisions, cells undergo a series of transitions in nuclear organization, which serve to identify and pair homologous chromosomes. This is followed by the stabilization of chromosome pairing interactions, often in the context of a highly structured protein scaffold known as the synaptonemal complex (SC). In most organisms, including fungi, plants, mice and humans, homolog pairing initiates with telomeres clustering at the nuclear envelope. This chromosomal configuration is known as the bouquet because it lends a distinctive shape to the chromosome assembly [1]. Similarly, in worms, the tethering of special telomere-proximal chromosomal regions near the nuclear envelope assists the pairing of homologues and SC formation (synapsis) [2]. By contrast, no bouquet stage is observed in *Drosophila*, which interestingly lack traditional telomeres. However, *Drosophila* oocytes have long been known to form another structure at this stage in meiosis called the chromocenter, which is composed of clustered centromeres [3,4]. Two studies from the Hawley and McKim laboratories [5,6], published in a recent issue of *Current Biology*, now reveal some intriguing functional parallels between the *Drosophila* chromocenter and the bouquet, and designate the chromocenter as the structure where synapsis first begins.

The two groups arrived at their shared conclusion that the chromocenter initiates synapsis from somewhat different starting points. Hawley and colleagues [5] investigated the genetic basis of centromere clustering, which they noted occurs very early during oogenesis, whereas McKim and colleagues [6] were establishing a time course of chromosome synapsis in *Drosophila* oocytes. Both groups analyzed C(3)G, a protein that forms part of the 'rungs' that connect homologous chromosomes in the context of the SC. The key characterization made by both groups was that early in meiosis, C(3)G formed only a couple of foci on chromosomes, and these foci co-localized perfectly with centromere clusters (Figure 1A). Only at later stages did C(3)G also coat non-centromeric sites, suggesting that the centromeres act as the earliest sites of synapsis initiation in *Drosophila* oocytes. In some organisms, including worms and grasshoppers, synapsis only initiates at one or two sites along each chromosome, most commonly near the telomeres. This is not the case in *Drosophila*. As demonstrated in a careful analysis by McKim and colleagues, C(3)G forms clearly distinguishable patches along chromosomes rather than a single widening stretch, indicating that synapsis also initiates at interstitial chromosomal sites (Figures 1B–D). What defines these interstitial sites is unclear, but in budding yeast and mice, interstitial sites of synapsis are thought to be associated with sites of homolog identification.

Interestingly, many components of the SC are required for centromere clustering in the first place, suggesting that synapsis initiation and centromere clustering are tightly coupled. Analysis of mutations in SC components by Hawley and colleagues revealed that many exhibited strong defects in centromere clustering. Moreover, both groups showed that the meiotic chromosome cohesion protein ORD is essential for centromere clustering and the initial synapsis at centromeres. One interesting exception is the SC

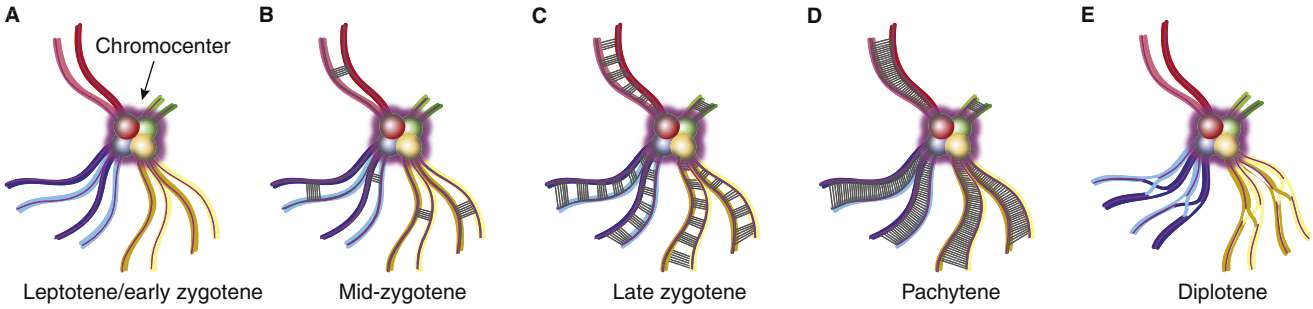

Figure 1. Synapsis progression in *Drosophila* oocytes.

(A) SC proteins first appear at centromeres concomitantly with chromocenter formation in leptotene/early zygotene. Centromere clustering in the chromocenter is dependent upon cohesion proteins, ORD and SMCs (shown in purple), as well as SC components, C(3)G and Cona (shown in grey). (B) In mid-zygotene, a few patches of SC are also visible on the chromosome arms. (C) Arm-associated SC patches become more numerous by late zygotene, until chromosomes are fully synapsed in pachytene (D). (E) In diplotene, the SC disassembles along chromosome arms and homologous chromosomes are linked by chiasmata (the cytological manifestations of crossovers). The X chromosome (red) and the fourth chromosome (green) are achiasmate in this schematic. The SC proteins persist at the centromeres in diplotene oocytes and may assist in the segregation of achiasmate chromosomes. (Figure courtesy of Tom DiCesare, Whitehead Institute.)

component C(2)M, which appears to be of lesser importance for centromere coupling. The results of the two groups differ somewhat in this respect, with Hawley and colleagues finding partially reduced centromere clustering in *c(2)M* mutants, whereas McKim and colleagues report no effect on centromere clustering when analyzing the same mutants. Although further analysis will be necessary to clarify this point, the finding that C(2)M is less important for centromere clustering than other SC components is interesting because it contrasts with the strong requirement of C(2)M for synapsis initiation at interstitial sites [6]. A differential requirement for C(2)M meshes well with previous ultrastructural data, which indicated that the structure of the SC differs between centromeres and chromosome arms [3]. The finding that both cohesion and synapsis are required for centromere clustering is also highly reminiscent of the requirement of SC components and cohesion proteins for bouquet formation in mice [7], reinforcing the notion that the *Drosophila* chromocenter is in many ways analogous to the bouquet.

Two additional intriguing findings emerged from these studies. The first is an apparent fluidity of the SC, revealed by a set of elegant experiments by McKim and colleagues [6]. They induced expression of an epitope-tagged version of C(2)M in adult females and found that the tagged protein was integrated into the SC of fully synapsed oocyte chromosomes. C(2)M is required to build the lateral elements of the SC on which the C(3)G-containing rungs are assembled, and thus would not be expected to be easily exchanged without turnover of the entire structure. The SC had long been assumed to be a rigid structure because of its high structural regularity in electron microscopic images. These new observations strongly challenge this view, indicating instead that the SC remains dynamic, even when fully assembled between homologous chromosomes. Future studies will undoubtedly shed more light on this unexpected feature of the SC.

The second exciting observation is the finding by Hawley and colleagues [5] that SC components persist on clustered centromeres well past the disassembly of the SC on chromosome arms (Figure 1E). A similar persistence of SC components at centromeres or telomeres after SC disassembly has been observed in a number of organisms, including budding yeast and rats [8,9]. Although the significance of this process during *Drosophila* oogenesis is not clear, one possibility is that SC components at clustered centromeres promote proper segregation of achiasmate chromosomes. Achiasmate chromosomes result when the process of meiotic recombination, which occurs concurrently with SC formation, fails to form a crossover between a pair of homologous chromosomes (Figure 1E). Because crossovers normally provide the physical linkages that allow homologous chromosomes to align in the metaphase plate of the first meiotic division, achiasmate chromosomes are at an increased risk of missegregation. The persistence of SC components at centromeres, with their ability to connect homologous chromosomes, may thus provide a back-up mechanism that keeps achiasmate homologues together. Such a function was recently reported for the SC protein Zip1 in budding yeast [10,11] and has also been suggested to regulate the segregation of the achiasmate XY chromosome pair of the marsupial *Thylamys elegans* [12]. Indeed, the recent observation that several *ord* mutations affect achiasmate segregation in *Drosophila* [13] may be consistent with this model. It will be interesting to see whether the severity of the achiasmate segregation defects of these *ord* mutants is correlated with a loss of C(3)G from centromeres and weakened centromere clustering.

The synaptonemal complex has been a very attractive structure for cell biologists, biochemists and geneticists alike. More than 50 years after its discovery, the SC is still an enigma. Further research such as described in these two studies should get us closer to understanding the various roles and complexities of the synaptonemal complex.

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Organelle Dynamics: ER Embraces Mitochondria for Fission

The endoplasmic reticulum and mitochondria are engaged in an intimate relationship: they establish extensive contacts, exchange lipids and calcium, and coordinate their activities in cell life and death. Recent research has revealed a new role for the endoplasmic reticulum in promoting mitochondrial division.

Benedikt Westermann

Cellular organelles were long regarded as separate entities that provide secluded compartments tailored for specific cellular or metabolic reactions. This view has changed as it has been recognized that organelles are highly dynamic and interdependent. It is now becoming clear that the intricate architecture of a eukaryotic cell can be established and maintained only through coordinated and cooperative activity of its constituents. Now, in a recent article published in *Science*, Friedman *et al.* [1] report that the endoplasmic reticulum (ER) plays an active role in defining the sites of mitochondrial division and thereby helps to shape the mitochondrial compartment.

Mitochondria are highly dynamic organelles that frequently fuse and divide. This dynamic behaviour determines mitochondrial morphology and serves many important functions [2]. The formation of large, interconnected mitochondrial networks by the fusion of individual organelles facilitates the transmission of the mitochondrial membrane potential to dissipate metabolic energy. It also allows intermixing and exchange of mitochondrial content and complementation of mitochondrial gene products, a process thought to counteract the decline of mitochondrial functions during aging. Mitochondrial fission, on the other hand, is required to generate organelles that are small enough to be transported by molecular motors along the cytoskeleton. This is particularly important in large, differentiated cells, such as neurons, and during cell division. Moreover, mitochondrial fission is important for the release of cytochrome *c* from the mitochondrial intermembrane space into the cytosol to trigger apoptosis, and it is thought to facilitate the removal of damaged organelles by autophagy [2]. Given this multitude of cellular functions, it is not surprising that defects in mitochondrial fusion and fission are associated with several diseases, including age-associated neurodegeneration or neonatal death [2].

The key protein mediating mitochondrial division is an evolutionarily conserved dynamin-related protein called Dnm1 in yeast or Drp1 in mammals. Members of the dynamin family are large GTPases that self-assemble into large helical oligomers that wrap around cellular membranes. Membrane tubulation and/or fission is then achieved by mechanochemical forces released upon GTP hydrolysis [3]. The molecular machinery of mitochondrial fission has been studied in great detail, both in yeast and in mammals. In yeast, a mitochondrial outer membrane protein, Fis1, and a soluble adaptor protein, Mdv1, promote the assembly of cytosolic Dnm1 on the mitochondrial surface, driving membrane scission [4–6]. Similarly, mammalian Drp1 can be recruited to the mitochondrial surface by Fis1, albeit without the participation of an Mdv1 homologue [7]. In addition, the outer membrane of mammalian mitochondria contains a Fis1-independent division protein, Mff, which recruits Drp1 and is essential for mitochondrial fission [8,9]. Although these and many other studies provided a wealth of data allowing detailed insights into the mechanics of mitochondrial division, two major questions remained unanswered. First, Dnm1 was observed to assemble on many sites on yeast mitochondria, but not every Dnm1 oligomer was found to promote a mitochondrial fission event [10]. Thus, it is not known how the mitochondrial division sites are selected from the Dnm1 assembly sites. And second, the diameter of Dnm1 helices assembled on lipid tubes *in vitro* (~100 nm) is much smaller than the diameter of a typical mitochondrial tubule (~300 nm) [6]. So how can