modulation: High frequency gamma activity was stronger in primary motor cortex contra-lateral to the responding hand (compared to ipsi-lateral motor cortex), whereas low frequency (<40 Hz) activity showed the opposite pattern. These results are consistent with previous studies that show movement related increases in high frequency bands and suppressions in low frequency bands [10–12].

Having identified these two 'markers', Donner *et al.* [1] could track the evolution of these markers during presentation of the moving dots. Interestingly, this novel approach revealed that the amplitude of both components during stimulus presentation — well before movement onset — predicted subsequent responses. The prediction accuracy of the markers increased towards the end of the stimulus presentation period. These findings indicate that the temporal dynamics of the decision process are reflected in motor areas.

To elucidate the mechanisms of the decision process in more detail, Donner *et al.* [1] analysed the two identified markers at the back-end stage of the decision process in more detail. They found that even in trials where participants did not perceive coherent motion predictive activity in the motor areas can be observed as early as in trials where participants did perceive coherently moving dots. This result argues against a simple decision process whereby subjects decide that they perceive the motion if the sensory evidence for the target surpasses a certain threshold. Finally, the authors related their gamma decision-marker at the output stage of the decision process to neuronal gamma oscillations at the sensory level — in the motion-sensitive area MT. Analysing single trials, they observed that the temporal integral of gamma-activity in MT was significantly correlated with the strength of lateralized gamma activity in motor cortex throughout the stimulation period (Figure 1, middle column). This finding provides compelling evidence (albeit only in four participants) for the temporal integration model outlined above in humans (Figure 1, right panel).

Taken together, these recent studies open a new window to the understanding of simple perceptual decision processes. However, several questions remain to be answered: To what extent are motor areas involved in decisions where no overt motor response is required? Where and how is the sensory evidence provided by lower-level brain areas integrated and transformed to a motor plan? To answer these questions future studies will likely combine sophisticated analysis techniques such as distributed source localization, spectral analysis, functional connectivity analysis, single-trial and machine learning analysis to optimally exploit the high temporal resolution of MEG/EEG.

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Meiosis: Making a Synaptonemal Complex Just Got Easier

In preparation for meiosis, chromosomes go through several massive structural transitions, including chromosome fragmentation, pairing and synapsis. A checkpoint factor and a SUMO ligase collaborate to keep things in order.

Andreas Hochwagen

Meiotic prophase is a busy period for chromosomes. Within a comparatively short time, chromosomes become duplicated, undergo controlled fragmentation and reshuffling during meiotic recombination, and finally end up paired and synapsed along their entire lengths by the synaptonemal complex [1–3]. Not surprisingly, the proper timing and coordination of these events is key to avoiding chromosome abnormalities and meiotic defects.

One particularly interesting problem is the formation of the synaptonemal complex. A favorite of cell biologists for many decades, the synaptonemal complex is an elaborate protein superstructure that apposes and links pairs of homologous chromosomes. By electron microscopy, the synaptonemal complex appears like a train track that assembles in a zipper-like fashion to keep chromosomes arranged at a set distance from each other (Figure 1) [1,3].

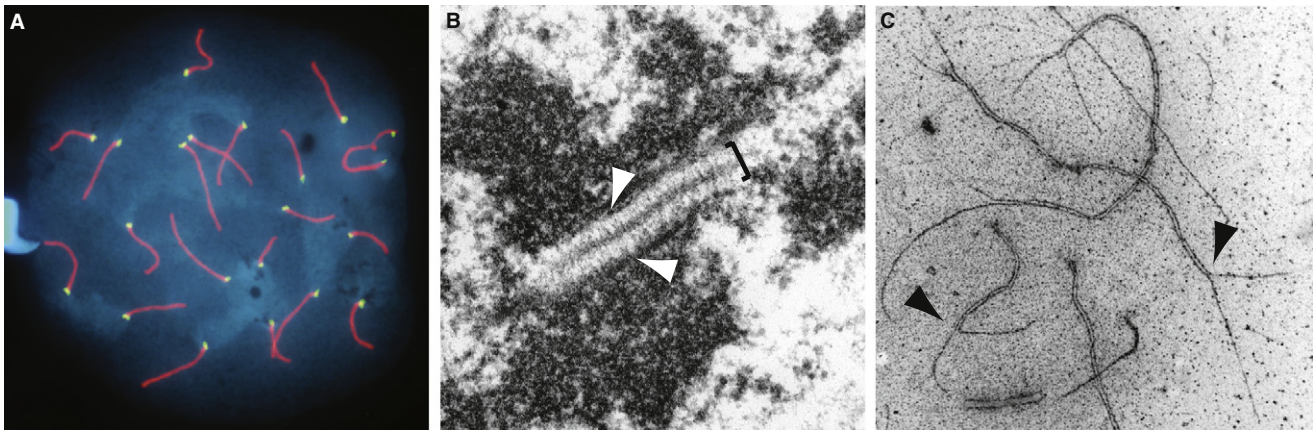

Figure 1. The synaptonemal complex.

(A) Fully synapsed chromosomes of a mouse spermatocyte. DNA is stained blue, the synaptonemal complex protein SYCP3, red, and centromeres, green. (B) Electron micrograph of a synaptonemal complex from rat spermatocytes showing the train track arrangement of chromatin-associated, electron-dense lateral elements (arrowheads) bridged by zipper-like transverse filaments (bracket). (C) Electron micrograph of ongoing synapsis (black arrowheads) in the grasshopper *Paratettix meridionalis*. Images were generously provided by Julio Sanchez Rufas, Madrid (A); Manfred Alsheimer and Ricardo Benevente, Würzburg (B); and Juan Luis Santos Coloma, Madrid (C).

Chromosome synapsis follows a fixed temporal pattern and its initiation in many organisms is directly coupled to chromosome fragmentation [4–6]. In some cases, the coupling of fragmentation and synapsis appears rather straightforward. For example, in the budding yeast *Saccharomyces cerevisiae* and the fungus *Sordaria macrospora*, the chromosome breaks themselves serve as sites of synapsis initiation [3,4]. However, other organisms, including grasshoppers, worms and humans, often only have a single site of synapsis initiation per chromosome [7–9], making the potential coupling mechanisms less obvious. Indeed, even in budding yeast the situation is not quite as simple. Yeast centromeres are potent sites of synapsis initiation not associated with chromosome breaks [10]. Strikingly, despite this apparent break-independence, synaptonemal complex assembly at centromeres does not start until meiotic chromosome fragmentation has initiated across the genome, raising the question of how break formation and synapsis are coordinated in this situation.

The identification of the proline isomerase Fpr3 and the SUMO ligase Zip3 as suppressors of centromeric synapsis initiation in budding yeast, reported by MacQueen and Roeder [11] in this issue of *Current Biology*, is shedding some new light on this problem. Remarkably, yeast mutants lacking both factors initiate synaptonemal complex assembly even in the absence of chromosome breaks.

This finding has several important implications. Most immediately, it indicates that the synapsis machinery is operative but actively inhibited as long as breaks have not formed. As the authors point out, such conditional coupling of two processes fits the general definition of a checkpoint mechanism. That is, the onset of one process (synapsis) is contingent on the completion of another (break formation) without being physically dependent on it (synapsis can also occur in the absence of breaks). Already, several checkpoints are known to act in meiotic prophase [12], suggesting that such coupling mechanisms are an effective strategy for coordinating the various meiotic chromosome transitions.

Equally remarkable is the identification of Fpr3 and Zip3 as suppressors of synapsis, and thus, effectively, as checkpoint factors. Zip3, in particular, came as a surprise because it had previously been thought of as an activator, rather than a suppressor, of synapsis [13,14]. This earlier conclusion came from the analysis of synapsis initiation at chromosome breaks, which is dramatically impaired in the absence of Zip3 [13]. How could these different functions be reconciled? One interpretation offered by the authors is that Zip3 sumoylates different targets at break sites and at centromeres leading to different and opposing effects on synapsis. Alternatively, the substrate may be the same but the requirements for synapsis initiation may differ between break sites and centromeres. Indeed, several synaptonemal complex components require Zip3 for localization to chromosome breaks but not to centromeres [10].

The apparent role of Fpr3 in synapsis control is no less intriguing. Fpr3 had previously been identified as a checkpoint factor required for the response to persistent unrepaired chromosome breaks [15]. Now, it appears the response to a *failure* in break formation also requires Fpr3. Despite these different defects, the role of Fpr3 in both processes from a mechanistic point of view is not dissimilar. In both situations, Fpr3 basically serves to put cells on hold. In the response to persistent breaks, Fpr3 prevents premature adaptation and exit from meiotic prophase. Similarly, Fpr3 prevents premature synapsis initiation when breaks have not yet formed. Perhaps, rather than directly responding to the defects, Fpr3's role in meiotic checkpoint control is more general. One possibility is that Fpr3 in some way serves as a molecular 'speed bump' that slows meiotic progression and buys time for various problems to be rectified.

Once breaks have formed, how is the block to synapsis alleviated? An immediate candidate is the DNA damage checkpoint machinery, which is always activated upon chromosome

break formation [12] and could act as a signaling mechanism. It will be interesting to see whether checkpoint kinase activation can trigger synapsis initiation at centromeres.

Another obvious question concerns the importance of this coupling mechanism. Indeed, although the coupling of synapsis to chromosome fragmentation is widely conserved, it is not a general phenomenon, and a number of organisms, including flies and nematodes, undergo meiosis successfully without this additional level of control [1,3]. A possible clue lies in the fact that synaptonemal complex formation does not *a priori* occur between homologous chromosomes. Non-homologous synapsis is observed in a variety of situations where homology search is impeded or impossible, including inversion heterozygotes and haploids [3]. Thus, meiotic cells need mechanisms to ensure that synapsis only initiates between homologous chromosomes. Interestingly, in budding yeast and mice, where coupling of synapsis and chromosome fragmentation is observed [3,6], the exposed chromosome breaks provide the primary means to identify homology and align matching homologous chromosomes [16]. In contrast, flies and nematodes are highly proficient in homolog alignment even without chromosome fragmentation [16,17]. In flies, homologous chromosomes are aligned not only in the germ cells, but also in practically all somatic cells of the adult organism [17]. Nematodes, on the other hand, have chromosome-specific pairing centers at the ends of all chromosomes that identify homologous chromosomes in the absence of chromosome fragmentation [9,16]. Hence, an intriguing correlation emerges, whereby organisms that require chromosome breaks for homology search couple synapsis initiation to break formation, whereas organisms with break-independent pairing mechanisms do not.

Finally, if coupling synapsis initiation to chromosome fragmentation is so important in budding yeast, why not dispense with centromeric initiation sites altogether and make chromosome breaks the exclusive nucleation sites? It is possible that centromeres provide a backup mechanism. Because every chromosome has a centromere, this setup would ensure synapsis on chromosomes that failed to undergo chromosome fragmentation. In this context it is worth noting that even in the absence of synaptonemal complex zippering, the presence of synaptonemal complex components at centromeres is sufficient to tether pairs of centromeres together [18]. Although this coupling is non-homologous, it may assist with the correct alignment of individual pairs of homologous chromosomes, for which homology search failed.

Clearly, the current work has raised many new and intriguing questions and is bound to inspire further investigations into the complexities of synapsis.

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Vision: Thinking Globally, Acting Locally

The global structure of images profoundly influences how we see their local detail, consistent with activity in primary visual cortex being *disambiguated* via feedback from later visual areas.

Steven C. Dakin

In this issue of *Current Biology*, Warren and Rushton [1] describe how the direction in which we see objects move can be strongly influenced by movement of the surrounding scene, in a manner that is consistent with the brain attempting to discount the disruptive influence of our own movement. This suggests that known neural mechanisms sensitive to *optic flow* — the patterns of visual motion that arise under self-motion — may be