

## Review

## Landscaping Crossover Interference Across a Genome

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The evolutionary success of eukaryotic organisms crucially depends on the capacity to produce genetic diversity through reciprocal exchanges of each chromosome pair, or crossovers (COs), during meiosis. It has been recognized that COs arise more evenly across a given chromosome than at random. This phenomenon, termed CO interference, occurs pervasively in eukaryotes and may confer a selective advantage. We describe here a multipoint linkage analysis procedure for segregating families to quantify the strength of CO interference over the genome, and extend this procedure to illustrate the landscape of CO interference in natural populations. We further discuss the crucial role of CO interference in amplifying and maintaining genetic diversity through sex-, stress-, and age-induced differentiation.

## Meiotic COs and Interference

Meiosis, a specialized type of cell division used by sexually reproducing organisms, reduces the chromosomal complement by half to generate haploid gametes from diploid cells. During meiotic prophase, two homologous chromosomes, each from a different parent, exchange genetic material, leading to recombinant chromosomes. This phenomenon, known as crossing over, together with **independent assortment** (see [Glossary](#)) of chromosomes, constitute two important mechanisms by which meiosis promotes genetic diversity and ensures that each gamete inherits a copy of every chromosome [1–4]. Because the exchange occurs between non-sister **chromatids**, COs allow genes from each parent to intermix, and thus form new chromosomes with a different genetic complement, resulting in new traits in offspring. In most organisms the number and distribution of COs are highly regulated by a pervasive mechanism, called CO interference or genetic interference, through which a CO discourages the formation of additional nearby COs by generating some CO-discouraging signal or substance that spreads some distance along the chromosome [5]. Because of such interference, **chiasmata** are more evenly placed along the **bivalents** than would be expected by chance [5,6].

CO interference is a universal phenomenon that has received a great deal of attention since its discovery over a century ago [7]. The extent of CO interference was observed to decrease with distance between COs, while, given the same distance, it is stronger on the same chromosomal arm than on two arms [5]. The strength of interference was thought to depend inversely on the physical distance separating the COs, but a body of evidence also shows that CO interference is more crucially contingent on genetic distance than on physical distance [8]. The distribution density of interference varies among different eukaryotes; for example, interference operates in tens of kb in budding yeast, tens of Mb in mice and humans [8,9], and 46 centimorgans (cM) in

## Trends

COs between two homologous chromosomes during meiosis promote genetic diversity, and are regulated by three machineries, (i) obligate CO formation, (ii) CO interference, and (iii) CO homeostasis.

CO interference, a phenomenon where the occurrence of one CO prevents the formation of another CO nearby, is detected traditionally by genetic mutation screening.

The identification of CO interference can also be through multipoint analysis. By designing various sampling strategies based on biological properties of species, this approach can be widely used to estimate and test CO interference for both experimental and natural populations.

Multipoint analysis, that is traditionally used to construct genetic linkage maps, provides a means to detect and quantify CO interference, thereby providing new insights into the mechanistic basis of genome evolution in eukaryotes.

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