Current Biology Vol 14 No 24
R1036

The team modelled three different scenarios: the loss of pollinators at random; the loss first of specialised pollinators then of more generalised pollinators; and vice versa, the loss of more generalised then more specialised pollinators.

Under their model, they found that random removal of pollinators elicited a steadily accelerating decline in plant species, with the bulk of plant extinctions occurring only after 70–80 per cent of all pollinator species had been lost. Their model for systematic removal beginning with the most specialised pollinators led to a scenario of a very slow loss of plant species until almost all pollinators had been removed, at which point plant species numbers dropped precipitously to zero. This was especially true in the Illinois work: plants in this network were virtually unaffected until removal of the last few most generalised pollinators, representing less than one per cent of the 1,430 total animal species. Finally, systematic loss beginning with the most generalised predators led to a more rapid loss of plant species, but in a linear manner.

The study highlights, in particular, the importance of generalised pollinators. In both the systems studied these core pollinators derive mainly from the insect orders Hymenoptera and Lepidoptera. Six families of bees, including bumble bees, form part of the core pollination group at both sites. The authors highlight the need for management decisions formulated in advance from the best available information. “These groups should be given high priority for research and management in an effort to conserve the pollination interaction in northern temperate ecosystems,” the authors report.

Quick guide

Crossover interference

Kenneth J. Hillers

What is crossover interference?

During prophase of meiosis in most eukaryotes, DNA recombination events between homologous chromosomes are induced to occur at high frequency, so there are usually multiple events per chromosome pair per meiosis. Whereas many of these recombination events are non-reciprocal, a subset results in reciprocal exchange of genetic material between chromosomes — crossovers, which in the presence of appropriate markers can be detected as linkage alterations. A genetic map is actually a map of the frequency and distribution of meiotic crossovers along a chromosome within a population. When researchers first began constructing genetic maps of *Drosophila* in the early part of the 20th century, they realized that the positions of multiple crossovers along a chromosome were not random with regard to each other. Muller observed that “the occurrence of one crossing-over interferes with the coincident occurrence of another crossing-over in the same pair of chromosomes, and I have accordingly termed this phenomenon ‘interference’”.

Interference has subsequently been shown to operate in most — but not all — eukaryotes assayed. Interference results in widely spaced crossovers along chromosomes. Most eukaryotes average only a few crossovers per chromosome pair per meiosis. This means that interference can exert its effect across whole chromosomes (or chromosome arms). As chromosomes in many eukaryotes are large, interference must be able to act over megabase lengths of DNA. Indeed, in the nematode *Caenorhabditis elegans*, interference is capable of acting over a fusion chromosome of 50 Mb — nearly half the genome!

How does interference work?

Interference, by definition, means that crossovers somehow discourage other crossovers from occurring nearby. One simple model for how interference works is that a crossover generates some crossover-discouraging signal or substance that then spreads for some variable distance along the chromosome on either side of the crossover. In this way, additional crossovers near the initial one would be infrequent, with the magnitude of the effect decreasing with increasing distance from the initial crossover. This model may indeed describe how interference works, but supporting evidence is scarce. Despite nearly a century of investigation we still don’t know how interference is exerted.

Interference acts over widely varying DNA lengths in different eukaryotes: tens of kilobases in budding yeast, and tens of megabases in mice and humans. Chromosome fusion and bisection studies have shown that interference within a specific chromosome region can vary depending on the overall size and structure of the chromosome. This variability suggests that interference is not a property of DNA itself.

Meiotic recombination occurs in prophase of meiosis. During this stage chromosomes assemble protein structures along their length: chromosome axes and the synaptonemal complex. Many models for interference have suggested that the synaptonemal complex, a proteinaceous structure that assembles between paired homologous chromosome axes, can in some way effect or mediate interference; recent evidence from a number of organisms, however, indicates that interference is exerted prior to assembly of the synaptonemal complex. These results and others support the idea that the meiotic axes — protein cores along which meiotic chromosomes condense — play a role in interference.

But how does interference work? Mathematical modeling has revealed that the observed

distribution of crossovers in some organisms fits very well with that expected if each crossover recombination event is separated by a fixed number of non-crossover recombination events, suggesting that cells may be able to 'count' recombination events. But although mathematically satisfying, this idea is (as yet) mechanistically unenlightening.

Another type of model suggests that meiotic chromosomes are under stress, for example as a result of changes in chromosome organization following axis assembly, and that this stress promotes the occurrence of crossovers. Each crossover event releases stress for a certain distance along the chromosome in each direction, in that way discouraging nearby crossovers (stress leads to crossovers which locally relieve stress, interfering with nearby crossovers, much the way that deadline stress leads to grant submission, which leads to relaxation that interferes with subsequent grant writing…). Interestingly, Muller's initial ideas regarding how interference works are similar. This model satisfactorily explains interference — and leads to other interesting ideas (see below) — but may prove difficult to test.

Why don't we know how interference works? The study of interference is challenging, for two main reasons. First, interference is fundamentally a phenomenon of populations. To see its effects, one must measure crossing over in multiple intervals simultaneously in a number of meiotic products — the more, the better. And second, in most instances interference manifests itself as a reduced frequency of adjacent crossovers, rather than their complete absence. In this way, interference is probabilistic rather than deterministic.

These facts have complicated our quest for understanding interference. The populational nature of the phenomenon makes genetic screens for mutations affecting interference challenging, because screening for mutants by monitoring interference *per se* would involve measuring meiotic crossing over in multiple intervals along a chromosome in numerous meiotic progeny for each individual screened. Consequently, genetic screens for interference mutants require a surrogate phenotype, which introduces additional complications.

Furthermore, many of the chromosomal proteins that are candidate mediators of interference also play a role in formation of crossovers, so the usual genetic strategy of eliminating candidate components by mutation also reduces or eliminates the very crossover events whose regulation one wishes to study. And finally, the probabilistic nature of the phenomenon means that examination of any individual recombinant chromosome does not by itself provide information about interference. Simply finding a chromosome wherein two crossovers occurred 'nearby' is not informative; instead one must determine the frequency with which such events occur, a much more significant undertaking.

Why does interference exist? Crossover recombination events between homologous chromosomes play an important role in directing proper meiotic chromosome segregation in most studied eukaryotes, including humans. So it is not surprising that crossing over during meiosis is subject to regulation of various forms. For example, most eukaryotes seem to have a means of ensuring that each pair of homologous chromosomes enjoys the crossover necessary to ensure proper meiotic segregation — the 'obligate crossover'.

This seems reasonable enough: if you need crossovers to segregate your chromosomes, it seems advisable to have a system to ensure each chromosome pair has at least one. But it is less clear why interference exists — why adjacent crossovers are discouraged. One possibility is that adjacent crossovers may adversely impact the segregation of a chromosome pair during meiosis — that interference itself provides a selective advantage for the organism.

An intriguing alternative is that 'interference' is not by itself advantageous, but is a byproduct of some other mechanism acting during meiosis. One specific possibility is that interference is a consequence of the mechanism through which eukaryotes ensure the obligate crossover per chromosome pair. For example, in the chromosome stress model, crossovers are promoted by stress along the chromosome; crossing over then releases that stress for some distance. A system that monitors stress levels along chromosomes could in effect determine whether each chromosome pair had at least one (obligate) crossover. Under this model, the release of stress along the chromosome is as a signal to the cell that a crossover has occurred; inhibition of nearby crossovers is a byproduct, rather than an end in itself. If true, this suggests another reason why the mechanism of interference remains obscure despite years of study: many researchers have assumed that interference is an active process, and designed experiments accordingly. If interference is, instead, an incidental consequence of some other aspect of meiosis, then an understanding of that aspect of meiosis may shed light on interference as well.

Where can I learn more?

Bishop, D.K., and Zickler, D. (2004). Early decision; meiotic crossover interference prior to stable strand exchange and synapsis. Cell *117*, 9-15.

Foss, E., Lande, R., Stahl, F.W., and Steinberg, C.M. (1993). Chiasma interference as a function of genetic distance. Genetics *134*, 681-691.

Kleckner, N., Zickler, D., Jones, G.H., Dekker J., Padmore R., Henle J., and Hutchinson, J. (2004). A mechanical basis for chromosome function. Proc. Natl. Acad. Sci. USA *101*, 12592-12597.

Muller, H.J. (1916). The mechanism of crossing over. Am. Nat. *50*, 193-221, 284-305, 350-366, 421-434. (available in PDF format from www.jstor.org)

van Veen, J.E., and Hawley, R.S. (2003). Meiosis: when even two is a crowd. Curr. Biol. *13*, R831-R833.

Biological Sciences, California Polytechnic State University, San Luis Obispo, California 93407, USA.