Chromosomal rearrangements and speciation

Loren H. Rieseberg

Several authors have proposed that speciation frequently occurs when a population becomes fixed for one or more chromosomal rearrangements that reduce fitness when they are heterozygous. This hypothesis has little theoretical support because mutations that cause a large reduction in fitness can be fixed through drift only in small, inbred populations. Moreover, the effects of chromosomal rearrangements on fitness are unpredictable and vary significantly between plants and animals. I argue that rearrangements reduce gene flow more by suppressing recombination and extending the effects of linked isolation genes than by reducing fitness. This unorthodox perspective has significant implications for speciation models and for the outcomes of contact between neospecies and their progenitor(s).

Most species of plants and animals differ in their KARYOTYPES[1,2] (see Glossary). This observation, combined with evidence that chromosomal rearrangements might reduce the fertility of heterozygous hybrids (Box 1), has led some researchers to argue for a causative role for chromosomal change in SPECIATION[1,3]. For example, White concludes[1] that chromosomal rearrangements have 'played the primary role in the majority of speciation events'. The opposing and more widely held view is that the accumulation of chromosomal differences between populations is largely incidental to speciation[4–6].

The most widely cited reasons for doubting an important role for karyotypic change in speciation include: (1) the observation that many chromosomal rearrangements have little effect on fertility[5,7,8]; (2) theoretical difficulties associated with fixing chromosomal rearrangements that are strongly UNDERDOMINANT (i.e. reduce the fitness of heterozygotes)[9,10]; (3) the supposed ineffectiveness of chromosomal differences as barriers to gene flow[4,11,12]; and (4) the widespread belief that premating and/or ecological barriers arise earlier than chromosomal rearrangements in the speciation process and thus are more likely to cause speciation[6,13,14].

Here, I discuss prominent models of chromosomal speciation and population genetic issues associated with the establishment and spread of chromosomal rearrangements, and consider the validity of these models, particularly with respect to the effects of chromosomal rearrangements on the fitness of plant and animal hybrids and on interspecific gene flow. I argue that chromosomal rearrangements reduce gene flow more often through their effects on recombination rates than through their effects on fitness. I conclude by discussing the implications of this non-traditional view of chromosomal rearrangements with respect to: (1) traditional chromosomal speciation models; (2) SYMPATRIC or PARAPATRIC models of speciation; and (3) the survival of NEOSPECIES that have come back into contact with their progenitor(s).

Loren H. Rieseberg
Dept of Biology, Indiana University, Bloomington, IN 47405, USA.
e-mail: lriesebe@indiana.edu

Models of chromosomal speciation

There are many overlapping, largely untested, models of chromosomal speciation[3] (Box 2). These models share one fundamental feature: chromosomal differences that have accumulated between the neospecies and its progenitor(s) are assumed to impair the fertility or viability of interspecific hybrids (Box 1), thereby reducing gene flow[15]. However, almost all other assumptions vary between models (Table 1), including whether geographical isolation is required for speciation, the proposed means by which chromosomal rearrangements arise and become fixed in populations, and the effects of individual rearrangements on the fitness of chromosomally heterozygous individuals. In addition, some models suggest that adaptive differences associated with the chromosomal repatterning might allow the neospecies to colonize new habitats (quantum model) or to invade the habitat of the parental form (stasipatric model).

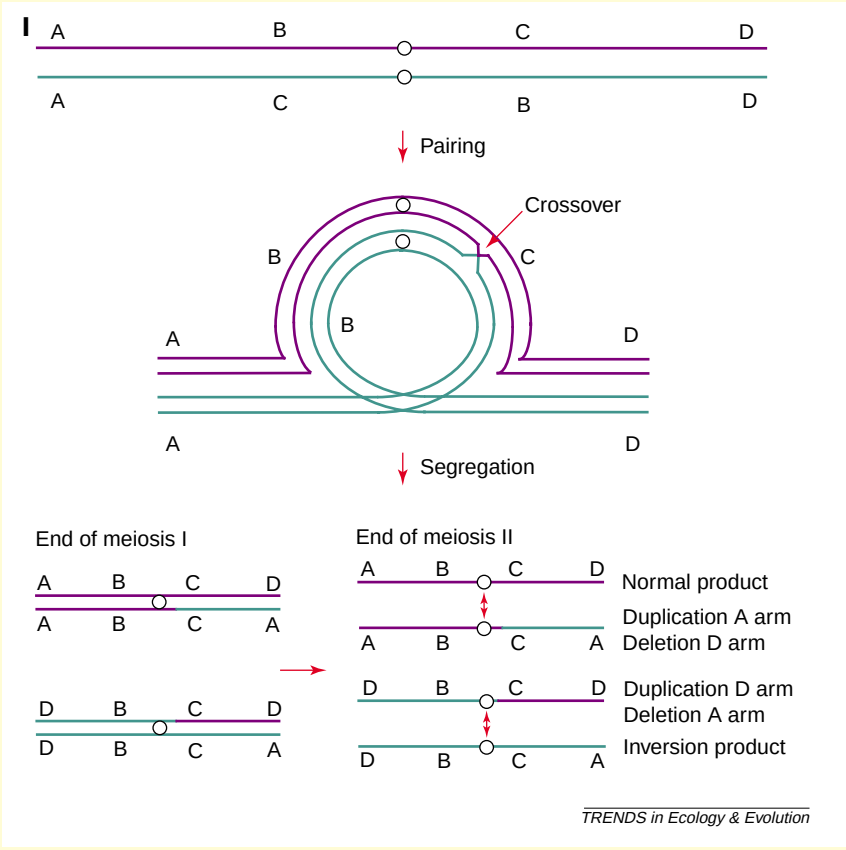
The primary difficulty with most chromosomal speciation models is that the fixation of strongly underdominant chromosomal rearrangements through drift is unlikely, except in small, inbred populations[9,10,15,16]. The difficulties associated with fixing underdominant mutations are exacerbated by SYMPATRY. Thus, it is unsurprising that most chromosomal models assume some sort of geographical isolation (Box 2; Table 1). Even hybrid or 'recombinational' speciation, which must be initiated in sympatry, is most probable when the hybrid neospecies becomes spatially isolated from its parental taxa following a hybrid founder event[17].

MEIOTIC DRIVE has been promoted as a complementary mechanism to drift for the fixation of rearrangements (stasipatric model), but it appears to be infrequent[18,19]. If chromosomal rearrangements are neutral or only weakly underdominant, the conditions required for their fixation are relaxed, but they are then less likely to reduce hybrid fitness. Only under special conditions, such as those outlined in the monobrachial centric fusion model[20], are rearrangements that were initially neutral likely to cause sterility in interpopulation hybrids. However,

http://tree.trends.com 0169–5347/01/$ – see front matter PII: S0169-5347(01)02187-5

Box 1. Chromosomal rearrangements and meiosis

There are several kinds of chromosomal rearrangement. These include the fusion or fission of chromosomes, the duplication or deletion of a chromosomal segment, the inversion of a segment and the translocation of segments between non-homologous chromosomes. In individuals that are heterozygous for one or more of these rearrangements, recombination between chromosomes that differ for the rearrangement(s) often generates UNBALANCED GAMETES (see Glossary) that might themselves die or that cause zygotes to die. In an example of a PERICENTRIC INVERSION (Fig. I; reproduced, with permission, from Ref. a), recombinant chromosomes resulting from a single crossover contain a duplication and a deficiency (small circles indicate centromeres). Gametes or zygotes with a recombinant chromosome might be inviable, leading to the selective recovery of non-recombinant chromosomes in viable offspring and an effective reduction in recombination.



Reference

a Griffiths, A.J.F. *et al.* (1993) *An Introduction to Genetic Analysis* (5th edn), W.H. Freeman & Co.

there is some evidence that rearrangements that are weakly underdominant individually might be strongly underdominant in combination[21] – the rationale that underpins cascade and chain models of chromosomal speciation (Box 2; Table 1). The recombinational model is immune to the problem of fixing underdominant rearrangements because hydridization brings them to a frequency of 50% and drift becomes incidental to the process. Unsurprisingly, the two models (monobrachial centric fusion and recombinational) that lack the theoretical problems associated with the fixation of underdominant mutations also provide the most convincing examples of chromosomal speciation in nature[22–24].

A related issue concerns the fitness of the novel chromosomal homozygote. If the new rearrangement is associated with a favorable gene complex, conditions for the establishment and spread of the rearrangement are slightly relaxed. However, the advantage with respect to establishment is present only when the population is small and selection against the underdominant mutation is weak[10]. As a result, homozygote advantage is rarely viewed as an important feature in the establishment of chromosomal rearrangements, but it is necessary for the migration of a new rearrangement into other populations (stasipatric model) and the colonization of habitats not occupied by the progenitor species (quantum model). With reference to the recombinational model (Table 1), new gene combinations arising from hybridization are assumed to contribute to ecological divergence[17], but the origin of these new gene combinations might be incidental to chromosomal repatterning.

A final consideration is the speed with which new chromosomal rearrangements arise and become established in populations[9,25] and the strength of the resulting sterility barrier. Most models rely on spontaneous mutation to drive chromosomal evolution but, in many taxa, this process will be slow relative to the development of ecological isolating barriers or the accumulation of genic sterility factors. Also, significant isolation will probably require multiple rearrangements[11,12], further slowing the process of chromosomal speciation. Two of the models listed in Table 1 (saltational and recombinational) suggest means by which multiple chromosomal rearrangements are fixed simultaneously and very early in the speciation process. In the saltational model[26], inbreeding induces chromosomal breakage, but there is little quantitative evidence for enhanced chromosomal mutation rates in inbred populations. The recombinational model[4,27] postulates that rapid karyotypic evolution occurs through the sorting of chromosomal rearrangements that differentiate the

Box 2. Models of chromosomal speciation

Many models of chromosomal speciation have been published over the past 50 years. Some of the most prominent models include:

- Chain or Cascade models, which assume that REPRODUCTIVE ISOLATION (see Glossary) arises via the accumulation of chromosomal rearrangements that are individually weakly underdominant[a].
- The Chromosomal Transilience model, which suggests that a strongly underdominant chromosomal rearrangement might become fixed through drift and inbreeding in an isolated population. REINFORCEMENT with respect to the ancestral KARYOTYPE might complete speciation[b].
- The Monobrachial Fusion model, which proposes that isolated subpopulations become independently fixed for different centric fusions, which individually cause little or no loss of fertility when heterozygous. However, hybrids between the two subpopulations would be intersterile because different combinations of chromosome arms had been fused in the two subpopulations[c].
- The Recombinational model , whichdescribes a process in which hybridization between chromosomal divergent populations leads to chromosomal breakage and to the sorting of preexisting rearrangements that differentiate the parental species. A new recombinant genotype could become stabilized if it is sufficiently karyotypically divergent (and thereby reproductively isolated) from either parental species[d].
- The Quantum speciation model, which suggests that chromosomal rearrangements might become fixed very rapidly in a peripheral founder population through drift and inbreeding, leading to reproductive isolation. This model is similar to the chromosomal transilience model except that the new gene arrangements resulting from karyotypic change are thought be adaptive[d].
- The Stasipatric model, which assumes that a strongly underdominant chromosomal rearrangement arises and becomes fixed in a population that is within the range of the progenitor species. Unlike other models, the stasipatric model postulates an important role for meiotic drive in the fixation of chromosomal rearrangements[a].
- The Saltational model, which proposes that inbreeding in a peripheral founder population could induce chromosomal breakage. However, as in most other models, chromosomal rearrangements (which later serve as isolating barriers) are fixed through drift in small, inbred populations[e].

References

a White, M.J.D. (1978) *Modes of Speciation*, W.H. Freeman & Co.
b Templeton, A.R. (1981) Mechanisms of speciation – a population genetic approach. *Annu. Rev. Ecol. Syst.* 12, 23–48
c Baker, R.J. and Bickham J.W. (1986) Speciation by monobrachial centric fusions. *Proc. Natl. Acad. Sci. U. S. A.* 83, 8245–8248
d Grant, V. (1981) *Plant Speciation*, Columbia University Press
e Lewis, H. (1966) Speciation in flowering plants. *Science* 152, 167–172

parental species and the accumulation of additional rearrangements induced by hybridization. Both of these mechanisms have contributed to karyotypic change in a strongly isolated hybrid sunflower species, *Helianthus anomalus*[24].

This discussion illustrates the paradox traditionally associated with chromosomal speciation[12]. Only rearrangements that are strongly underdominant are considered likely to contribute to speciation, but these kinds of rearrangements are exceedingly difficult to fix in natural populations. The monobrachial centric fusion and recombinational models are immune to this particular difficulty, but they are likely to be rare for other reasons. However, the effects of chromosomal rearrangements on gene flow – the parameter that really matters – are not necessarily strongly correlated with their effects on fertility. Moreover, in certain organismal groups, chromosomal sterility might evolve with sufficient relative speed to play an important role in the survival of neospecies that have come into contact with their progenitor(s).

Table 1. Differences among chromosomal speciation models

Model	Geographical isolation?	Mutational origins	Fitness of individual rearrangements	Means of establishment	Chromosomal repatterning adaptive?	Refs
Chain/Cascade	Yes	Spontaneous rearrangement	Weak underdominance	Drift	No	1
Chromosomal transilience	Yes	Spontaneous rearrangement	Strong underdominance	Drift	No	27
Monobrachial centric fusion	Yes	Spontaneous rearrangement	Weak or no underdominance	Drift	No	20
Recombinational	Probably	Hybridization	Weak or strong underdominance	Fertility selection	Maybe	2
Quantum	Yes	Spontaneous rearrangement	Strong underdominance	Drift	Yes	2
Stasipatric	No	Spontaneous rearrangement	Strong underdominance	Drift/meiotic drive	Yes	1
Saltational	Yes	Inbreeding	Strong underdominance	Drift	Maybe	26

Chromosomal rearrangements as isolating mechanisms

The impact of chromosomal rearrangements on hybrid fertility or viability is generally assumed to be synonymous with their effectiveness as barriers to gene flow. However, this is not necessarily the case. Rather, we need to consider two separate issues: (1) do chromosomal rearrangements affect hybrid fitness; and (2) can chromosomal rearrangements affect gene flow through mechanisms other than reduced hybrid fitness?

Effects on hybrid fitness

It has long been recognized that different kinds of chromosomal perturbations vary in their effects on fitness. For example, TRANSLOCATIONS, FUSIONS, FISSIONS and INVERSIONS are typically viewed as underdominant mutations, whereas HETEROCHROMATIN additions and deletions are not. Even supposedly underdominant rearrangements are unpredictable in their fitness effects because of the mechanisms that alleviate or prevent malsegregation at meiosis, such as partial or complete suppression of recombination[8].

There are two other relevant complications. First, it can be extremely difficult to distinguish between the effects of chromosomal rearrangements on hybrid sterility from those of genes[28]. For example, contrary to cytogenetic predictions, hybrids of chromosomally similar species sometimes exhibit abnormal meiotic pairing, whereas hybrids of chromosomally divergent species sometimes pair normally. Second, the effects of the same kinds of rearrangements appear to vary across organismal groups. In plants, for example, most rearrangements appear to have large effects on fertility[29], whereas in animals, karyotypic heterozygosity seems less likely to have negative fitness consequences[5,8].

This apparent difference between plants and animals with respect to chromosomal sterility was first recognized by Dobzhansky[7], who noted that the doubling of the chromosomal complement in plant hybrids typically led to a complete restoration of fertility. In *Drosophila* hybrids, however, chromosomal doubling failed to restore pairing or fertility. As explained by Dobzhansky, chromosomal doubling furnishes an exact homolog for each chromosome in the hybrid genome, thereby restoring pairing and fertility in chromosomally divergent hybrids. However, chromosomal doubling should have no effect on the action of complementary genes, so genic sterility is preserved. Based on this reasoning, sterility in *Drosophila* was interpreted as being caused by genes, whereas sterility in the referenced plant hybrids was assumed to be chromosomal in origin.

The conclusion that chromosomal rearrangements are more likely to contribute to the sterility of plants than to the sterility of animals is reinforced by additional evidence that has accumulated since these classic experiments[29,30]. This includes a much longer list of sterile plant hybrids that recover full fertility upon chromosomal doubling[29], as well as evidence that sterility in plants often maps to chromosomal rearrangements[31]. By contrast, sterility in animals (i.e. *Drosophila* and platyfish) has been mapped to genes[6,32]. A surprising observation is that sterile plant hybrids with normal pairing sometimes recover fertility following chromosomal doubling[29]. Sterility in these hybrids is interpreted as resulting from 'cryptic structural differentiation'. This has led to a paradoxical situation in which the burden of proof with respect to plant sterility is on those who interpret it as resulting from the action of genes, whereas for sterility in animals, the burden of proof falls onto those who argue for a chromosomal basis.

So why does chromosomal sterility appear to be more important in plants than in animals? One possibility relates to the observation that most genes are expressed in the male gametes of plants[33], but not of animals[34]. As a result, pollen carrying a deletion as a result of chromosomal irregularities will probably abort, whereas sperm are typically unaffected[35,36]. Female gametes of both plants and animals tend to be tolerant of deletions because of contributions of mRNAs and proteins from surrounding maternal tissue[36,37]. Although chromosomal deletions can cause the death of diploid offspring, many deficiencies are rescued by genes from the alternative gamete in newly formed zygotes. This reduces the fitness loss caused by chromosomal rearrangements, or at least defers the loss to later generations, making it more difficult to associate fitness reductions with chromosomal rearrangements.

A second possible explanation relates to the prevalence of differentiated sex chromosomes in animals versus plants. Most animals are dioecious and possess a degenerate Y chromosome, whereas most plants are hermaphroditic. Even in the small fraction of plants that are dioecious, Y-degeneration is minimal[38]. The degenerate Y makes most animals, but not plants, subject to HALDANE'S RULE, which states that if only one hybrid sex is sterile or inviable, it is always the heterogametic sex[39]. The accepted explanations for Haldane's rule are that most X-linked alleles that cause hybrid problems are partially recessive[40,41], and that genes that contribute to male sterility evolve more quickly than do those that cause female sterility[42]. The important point here is that genic sterility will evolve most rapidly in organisms with a large X chromosome and a very degenerate Y, such as *Drosophila*. By contrast, genic sterility is likely to evolve slowly in plants or in animals that lack a degenerate Y or that have only a small number of genes on the X chromosome. Rapid male evolution also seems most probable in organisms with differentiated sex chromosomes and thereby less constrained in their response to SEXUAL SELECTION[43]. The bottom line is that, although karyotypic changes might accumulate at similar rates in plants and animals, they will probably make a disproportionately large contribution to sterility in

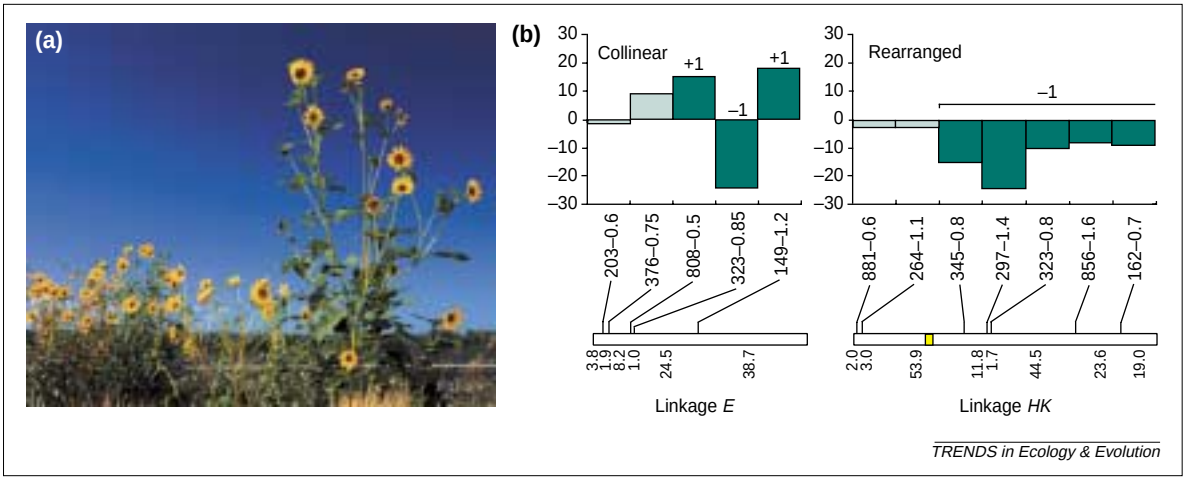


Fig. 1. Introgression in wild sunflower hybrid zones. (a) Photograph of *Helianthus petiolaris* (left), *H. annuus* (right), and F_1 hybrid (center). (b) Direct count deviations from the expected numbers of introgressed markers in three natural hybrid zones between *H. annuus* and *H. petiolaris*. Mapped molecular markers are given above and map distances below each linkage group. Independently selected chromosomal blocks are indicated by +1 or –1, depending on the direction of selection. The sizes of the independently selected chromosomal segments are indicated by a line above the data bars. Note that even very closely linked markers on the collinear linkage group (linkage *E*) introgress at very different rates, but that a very large linkage block behaves as a single unit on the rearranged linkage group (linkage *HK*) because of lower effective rates of recombination. Dark green, significant; light green, non-significant; yellow, translocation break point. Photograph reproduced, with permission, from Jason Rick. Fig. 1b reproduced, with permission, from Ref. 46.

plants because of the slower rate at which genic sterility evolves and because of gametic gene expression.

Effects on gene flow

The effects of chromosomal rearrangements on gene flow have been modeled on several occasions[11,12]. Gene flow near an underdominant locus declines in proportion to the selection:recombination ratio[11]. That is, weakly underdominant mutations will have essentially no effect on the flow of neutral genes, except for those closely linked to the rearrangement. The effects of strongly underdominant rearrangements will extend considerably further, even causing a modest reduction in the flow of unlinked, neutral genes. Multiple rearrangements have the effect of increasing the strength of selection against hybrids and increasing the proportion of genes that are tightly linked to a rearrangement and thus less likely to migrate[12]. Only with many rearrangements can a genome-wide barrier to introgression be ensured. Similar conclusions apply to genes that act in an underdominant fashion. However, these models have not investigated the role of chromosomal rearrangements in suppressing recombination. I argue that the suppression of recombination by chromosomal rearrangements[21,44] could be more important than their effects on fitness.

Except for geographical isolation, isolating mechanisms do not typically provide a complete barrier to gene flow between closely related species. Rather, species boundaries are often semipermeable, allowing neutral or advantageous alleles to move between species unless the alleles are tightly linked to loci that contribute in some way to isolation[11,45]. Species divergence is not necessarily halted by gene flow, because new mutations that are sensitive to genetic background or habitat, or that are tightly linked to 'isolation loci', can continue to accumulate. Thus, for many taxa, the unit of isolation is not the entire genome, but rather the chromosomal regions that harbor isolation loci. Under this paradigm, the effectiveness of an isolation locus is measured in terms of the length of the chromosomal segment that is partially or completely protected from gene flow.

Theoretical studies have not differentiated between the effects of genes and chromosomal rearrangements on gene flow, but empirical data suggest that there might be a large difference[46,47]. In three wild sunflower (*Helianthus*) hybrid zones (Fig. 1a), for example, rates of introgression were 50% lower across chromosomes carrying rearrangements than across collinear ones[46]. Isolation QUANTITATIVE TRAIT LOCI had small effects on the rates of introgression of markers as little as 1 cM away (Fig. 1b), but chromosomal rearrangements tended to suppress introgression across very large LINKAGE blocks (up to 100 cM). Similarly, it has been shown that regions of DNA just 2 kb from a sterility gene in *Drosophila* might act independently with respect to the retention of shared polymorphisms and/or history of introgression.

So why do we see a large difference in the effects of genes versus chromosomal rearrangements on the lengths of blocks protected from interspecific gene flow? The most probable explanation is that chromosomal rearrangements often suppress recombination and thereby restrict gene flow across larger genomic regions[48]. In some instances, the effective reduction in recombination could result from selection against recombinant gametes (Box 1), leading to lower hybrid fertility. In other cases, actual decreases in recombination frequency are observed without a loss of fertility[8]. Recombination suppression is typically associated with inversions[49,50], but there also is evidence for increased suppression of recombination around the CENTROMERES of Robertsonian heterozygotes in mice[51]. Rearrangements that suppress recombination, but lack a causal effect on hybrid fitness, could act synergistically with linked isolation genes to extend their effects over a larger genomic region. Thus, chromosomal rearrangements probably do play a major role in reducing gene flow across species barriers, but not necessarily through the mechanisms traditionally suggested[1].

Speciation and species interactions

The proposal that chromosomal rearrangements might reduce gene flow through their effects on recombination does not rescue most models of chromosomal speciation, because the restriction of gene flow across a large chromosomal block is a far cry from speciation. However, synergism between isolation genes and chromosomal rearrangements increases the plausibility of cascade or chain models. That is, several neutral or weakly underdominant rearrangements, if linked to isolation genes, could extend the effects of the latter over a larger fraction of the genome.

Speciation with gene flow

Chromosomal rearrangements might also facilitate certain modes in which speciation occurs in the presence of gene flow. Genetic models of this process indicate that the chief difficulty is recombination between a locus that causes ASSORTATIVE MATING and one or more loci subject to DISRUPTIVE SELECTION[52]. The suppression of recombination offered by chromosomal rearrangements increases the probability of these models[22,53,54], particularly in species whose number of chromosomes is small or in which the number of chromosomal rearrangements is large.

If rearrangements primarily influence speciation by reducing recombination rather than reducing fitness, is it possible that rearrangements become established because they alter recombination? Theoretical studies indicate that chromosomal rearrangements can be established if they reduce recombination between epistatically interacting genes, especially if the sex chromosomes are involved[55,56]. However, this argument seems less plausible for polymorphisms that segregate among populations because the selective advantage of the new rearrangement would be restricted to the zone of contact.

Species sorting

Chromosomal rearrangements might be most important through their mediation of contact between formerly allopatric species. It has been argued that, as peripheral neospecies expand their geographical distributions, they are likely to come into contact with their more widespread and more numerous progenitor(s)[57]. Only strongly isolated neospecies are likely to survive the challenge of sympatry; weakly isolated populations will merge with their progenitor(s) through hybridization. Chromosomal rearrangements might contribute to the required isolation, particularly for groups such as plants in which genic sterility evolves slowly. If this 'reproductive isolate selection' is common and chromosomal rearrangements are a major contributor, it might partially explain the disproportionate accumulation of chromosomal differences between rather than within species.

Both theoretical and empirical data indicate that reproductive isolate selection is probable in natural populations, but offer few clues about its frequency. The most relevant theoretical treatment[17] explores the conditions under which a hybrid neospecies could persist when parapatric with both parental species. The authors found that genetic isolation could be maintained if the chromosomal sterility barrier was strong and there was at least a small spatial gap between the neospecies and parental populations. If the sterility barrier was weakened or the gap size reduced, the hybrid neospecies either did not persist or became a component of a STEP CLINE in allele frequencies at loci under selection. Although the simulation was designed to study recombinational speciation (Table 1), these conclusions should be applicable to any neospecies that comes into contact with its progenitor(s).

Some recent empirical evidence is consistent with the concept of reproductive isolate selection. Much of the relevant information comes from the conservation biology literature, in which many examples of rare species threatened through hybridization have been documented[58]. With respect to the recombinational model, crossing experiments indicate that a natural hybrid sunflower species (*Helianthus anomalus*) is more strongly isolated from its parents (*H. annuus* and *H. petiolaris*) than are three synthetic hybrid LINEAGES[59]. This pattern might be a result of reproductive isolate selection (i.e. weakly isolated hybrid species were unable to persist), or could simply indicate that reproductive divergence has continued after speciation.

Conclusions and future directions

The effects of chromosomal rearrangements on the fitness of heterozygous hybrids appear to vary with respect to organismal group. They seem more likely to be a major cause of sterility in plants than in animals, perhaps because of differences in gene expression of male gametes and in sex determination. In the absence of a degenerate Y chromosome, genic sterility will evolve slowly, but the rate of karyotypic evolution should not be affected.

Even when chromosomal rearrangements have little or no effect on hybrid fitness, they might reduce gene flow through the suppression of recombination. By reducing recombination, rearrangements could act synergistically with isolation genes to diminish gene flow over much larger chromosomal regions than would otherwise be possible. This unorthodox mechanism increases the plausibility of cascade and chain models of chromosomal speciation, but for non-traditional reasons. Suppressed recombination caused by rearrangements might also facilitate sympatric and PARAPATRIC SPECIATION models that require LINKAGE DISEQUILIBRIUM between traits causing assortative mating and those under disruptive selection. More generally, chromosomal rearrangements might contribute to the survival of incipient peripatric species that have come into contact with their progenitor(s). Only strongly isolated neospecies will persist.

Of course, these ideas need to be confirmed experimentally. We need studies, for example, that examine the effects of different kinds of chromosomal rearrangements on recombination in a variety of different taxa and in both controlled crosses and natural settings. We also need to compare rates of introgression of molecular markers that occur at different distances from isolation genes and from chromosomal breaks. The prediction is that chromosomal rearrangements will protect longer chromosomal segments from interspecific gene flow than will isolation genes. To assess the validity of this prediction over a longer timescale, one could compare the genealogies of regions that are linked to rearrangements[60] or to isolation genes. Because of reduced recombination, GENEALOGICAL concordance should extend further from the chromosomal break than from the isolation genes. In addition to this empirical work, theoretical models that simulate the influence of variation in recombination patterns on gene flow would probably provide useful insights and allow a wider variety of evolutionary parameters to be explored.

To determine whether chromosomal rearrangements actually contribute to sympatric or parapatric speciation through recombination suppression, one could test whether assortative mating loci map proximal to chromosomal breakpoints as required by the model. Alternatively, one could ask whether speciation rates correlate more strongly with rearrangements that directly suppress recombination (e.g. inversions) than those that have only indirect effects on recombination (e.g. fusions). The question of whether chromosomal rearrangements contribute to reproductive isolate selection is more difficult to address. One kind of evidence that might be suggestive of chromosomal-based reproductive isolate selection, would be the disproportionate representation of chromosomal rearrangements in young versus old species. If chromosomal rearrangements do not frequently contribute to reproductive isolate selection, a more linear relationship between genetic and chromosomal divergence would be predicted.

In conclusion, considerable additional data will be required before the role of chromosomal rearrangements in speciation can be confidently evaluated. However, because of recent advances in genomics and molecular cytogenetics, conclusive experiments are now feasible and more confident answers should be forthcoming in the near future.

Acknowledgements
I thank N. Barton, K. Livingstone, A. Orr, J. Searle, M. Wade, T. Wood, and two anonymous referees for helpful comments on this article. My work on chromosomal rearrangements has been supported by the US National Science Foundation, the US Department of Agriculture and the National Institutes of Health.

References

1 White, M.J.D. (1978) *Modes of Speciation*, W.H. Freeman & Co.
2 Grant, V. (1981) *Plant Speciation*, Columbia University Press
3 King, M. (1993) *Species Evolution*, Cambridge University Press
4 Futuyma, D.J. and Mayer, G.C. (1980) Non-allopatric speciation in animals. *Syst. Zool.* 19, 254–271
5 Sites, J.W. and Moritz, C. (1987) Chromosomal evolution and speciation revisited. *Syst. Zool.* 36, 153–174
6 Coyne, J.A. and Orr, H.A. (1998) The evolutionary genetics of speciation. *Philos. Trans. R. Soc. London Ser. B* 353, 287–305
7 Dobzhansky, T. (1933) On the sterility of interracial hybrids in *Drosophila pseudoobscura*. *Proc. Natl. Acad. Sci. U. S. A.* 19, 397–403
8 Coyne, J.A. *et al.* (1993) The fertility effects of pericentric inversions in *Drosophila melanogaster*. *Genetics* 134, 487–496
9 Walsh, J.B. (1982) Rate of accumulation of reproductive isolation by chromosomal rearrangements. *Am. Nat.* 120, 510–532
10 Lande, R. (1985) The fixation of chromosomal rearrangements in a subdivided population with local extinction and colonization. *Heredity* 54, 323–332
11 Barton, N.H. (1979) Gene flow past a cline. *Heredity* 43, 333–339
12 Spirito, F. (2000) The role of chromosomal rearrangements in speciation. In *Endless Forms* (Howard, D.J. and Berlocher, S.H., eds), pp. 320–329, Oxford University Press
13 Schluter, D. (1998) Ecological causes of speciation. In *Endless Forms* (Howard, D.J. and Berlocher, S.H., eds), pp. 114–129, Oxford University Press
14 Schemske, D.W. (2000) Understanding the origin of species. *Evolution* 54, 1069–1073
15 Turelli, M. *et al.* (2001) Theory and speciation. *Trends Ecol. Evol.* 16, 330–343
16 Hedrick, P.W. (1981) The establishment of chromosomal variants. *Evolution* 35, 322–332
17 Buerkle, C.A. *et al.* (2000) The likelihood of homoploid hybrid speciation. *Heredity* 84, 441–451
18 Coyne, J.A. (1989) A test of the role of meiotic drive in chromosome evolution. *Genetics* 123, 241–243
19 Lenormand, T. *et al.* (1997) Chromosomal transmission bias in laboratory hybrids between wild strains of the two European subspecies of house mice. *Genetics* 147, 1279–1287
20 Baker, R.J. and Bickham, J.W. (1986) Speciation by monobrachial centric fusions. *Proc. Natl. Acad. Sci. U. S. A.* 83, 8245–8248
21 Searle, J.B. (1993) Chromosomal hybrid zones in eutherian mammals. In *Hybrid Zones and the Evolutionary Process* (Harrison, R.G., ed.), pp. 309–352, Oxford University Press
22 Piálek, J. *et al.* (2001) Raciation and speciation in house mice from the Alps: the role of chromosomes. *Mol. Ecol.*10, 613–626
23 Britton-Davidian, J. *et al.* (2000) Environmental genetics – rapid chromosomal evolution in island mice. *Nature* 403, 158
24 Rieseberg, L.H. *et al.* (1995) Hybrid speciation accompanied by genomic reorganization in wild sunflowers. *Nature* 375, 313–316
25 Lande, R. (1979) Effective deme sizes during long-term evolution estimated from rates of chromosomal rearrangement. *Evolution* 33, 234–251
26 Lewis, H. (1966) Speciation in flowering plants. *Science* 152, 167–172
27 Templeton, A.R. (1981) Mechanisms of speciation – a population genetic approach. *Annu. Rev. Ecol. Syst.* 12, 23–48
28 Shaw, D.D. *et al.* (1986) Estimating the genic and chromosomal components of reproductive isolation within and between subspecies of the grasshopper *Caledia captiva*. *Can. J. Genet. Cytol.* 28, 686–695
29 Stebbins, G.L. (1958) The inviability, weakness, and sterility of interspecific hybrids. *Adv. Genet.* 9, 147–215
30 Orr, H.A. (1996) Dobzhansky, Bateson, and the genetics of speciation. *Genetics* 144, 1331–1335
31 Rieseberg, L.H. *et al.* (2000) Hybridization, introgression, and linkage evolution. *Plant Mol. Biol.* 42, 205–224
32 Ting, C.T. *et al.* (1998) A rapidly evolving homeobox at the site of a hybrid sterility gene. *Science* 282, 1501–1504
33 Tanksley, S.D. *et al.* (1981) Evidence of extensive overlap of sporophytic and gametophytic gene expression in *Lycopersicon esculentum*. *Science* 213, 453–455
34 Hecht, N.B. (1998) Molecular mechanisms of male germ cell differentiation. *BioEssays* 20, 555–561
35 Morgan, D.T. (1950) A cytogenetical study of inversions in *Zea mays*. *Genetics* 35, 153–174
36 Griffiths, A.J.F. *et al.* (1993) *An Introduction to Genetic Analysis* (5th edn), W.H. Freeman & Co.
37 Stebbings, H. *et al.* (1995) Messenger-RNA translocation and microtubules – insect ovary models. *Trends Cell Biol.* 5, 361–365
38 Ainsworth, C. (2000) Boys and girls come out to play: the molecular biology of dioecious plants. *Ann. Bot.* 86, 211–221
39 Haldane, J.B.S. (1922) Sex-ratio and unisexual sterility in hybrid animals. *J. Genet.* 12, 101–109
40 Turelli, M. and Orr, H.A. (1995) The dominance theory of Haldane's rule. *Genetics* 140, 389–402
41 Presgraves, D.C. and Orr, H.A. (1998) Haldane's rule in taxa lacking a hemizygous X. *Science* 282, 952–954
42 Wu, C-I. and Davis, A.W. (1993) Evolution of postmating reproductive isolation: the composite nature of Haldane's rule and its genetic bases. *Am. Nat.* 142, 187–211
43 Fisher, R.A. (1930) *The Genetical Theory of Natural Selection*, Oxford University Press
44 Searle, J.B. (1998) Speciation, chromosomes, and genomes. *Genome Res.* 8, 1–3

45 Harrison, R.G. (1990) Hybrid zones: windows on evolutionary process. *Oxf. Surv. Evol. Biol.* 7, 69–128
46 Rieseberg, L.H. *et al.* (1999) Hybrid zones and the genetic architecture of a barrier to gene flow between two wild sunflower species. *Genetics* 152, 713–727
47 Ting, C.T. *et al.* (2000) The phylogeny of closely related species as revealed by the genealogy of a speciation gene, *Odysseus*. *Proc. Natl. Acad. Sci. U. S. A.* 97, 5313–5316
48 Rieseberg, L.H. *et al.* (1995) Chromosomal and genic barriers to introgression in *Helianthus*. *Genetics* 141, 1163–1171
49 Greenbaum, I.F. and Reed, M.J. (1984) Evidence for heterosynaptic pairing of the inverted segment in pericentric inversion heterozygotes of the deer mouse (*Peromyscus maniculatus*). *Cytogenet. Cell Genet.* 38, 106–111
50 Hale, D.W. (1986) Heterosynapsis and suppression of chiasmata within heterozygous pericentric inversions of the Sitka deer mouse. *Chromosoma* 94, 425–432
51 Davisson, M.T. and Akeson, E.C. (1993) Recombination suppression by heterozygous Robertsonian chromosomes in the mouse. *Genetics* 133, 649–667
52 Felsenstein, J. (1981) Skepticism towards Santa Rosalia, or why are there so few kinds of animals. *Evolution* 35, 124–138
53 Trickett, A.J. and Butlin, R.K. (1994) Recombination suppressors and the evolution of new species. *Heredity* 73, 339–345
54 Hauffe, H.C. and Searle, J.B. (1993) Extreme karyotypic variation in a *Mus musculus domesticus* hybrid zone – the tobacco mouse story revisited. *Evolution* 47, 1374–1395
55 White, M.J.D. (1973) *Animal Cytology and Evolution*, Cambridge University Press
56 Charlesworth, D. and Charlesworth, B. (1980) Sex differences in fitness and selection for centric fusions between sex chromosomes and autosomes. *Genet. Res.* 35, 205–214
57 Levin, D.A. (2000) *The Origin, Expansion, and Demise of Plant Species*, Oxford University Press
58 Rhymer, J.M. and Simberloff, D. (1996) Extinction by hybridization and introgression. *Annu. Rev. Ecol. Syst.* 27, 83–109
59 Rieseberg, L.H. (2000) Crossing relationships among ancient and experimental sunflower hybrid lineages. *Evolution* 54, 859–865
60 Andolfatto, P.A. (2001) Inversion polymorphisms and nucleotide variability in *Drosophila*. *Genet. Res.* 77, 1–8

Gene trees and species trees are not the same

Richard Nichols

The relationship between species is usually represented as a bifurcating tree with the branching points representing speciation events. The ancestry of genes taken from these species can also be represented as a tree, with the branching points representing ancestral genes. The time back to the branching points, and even the branching order, can be different between the two trees. This possibility is widely recognized, but the discrepancies are often thought to be small. A different picture is emerging from new empirical evidence, particularly that based on multiple loci or on surveys with a wide geographical scope. The discrepancies must be taken into account when estimating the timing of speciation events, especially the more recent branches. On the positive side, the different timings at different loci provide information about the ancestral populations.

Richard Nichols
School of Biological Sciences, Queen Mary, University of London, London, UK E1 4NS.
e-mail: r.a.nichols@qmw.ac.uk

Molecular PHYLOGENETICS (see Glossary) is based on the principle that the number of substitutions that have accumulated between the DNA sequences of two species indicates the time since their common ancestor. There is a fundamental problem with this approach, widely acknowledged in the standard texts (e.g. Ref. 1): the time back to the common ancestor of the two DNA sequences is typically longer than the time back to the common ancestor of the two species. The difference between the two times is shown as T_1 in Box 1. The molecules are most unlikely to have a common ancestor living at the very moment that the ancestral species split in two. Rather, the period T_1 is the time back to the common ancestor of the two molecules within the single ancestral species.

The timing of the SPECIATION events estimated from molecular phylogenies must be corrected for this bias, corresponding to the average value of T_1, and for the uncertainty owing to the variation around this average. These issues are important if the timing of speciation events is used to draw conclusions about the nature of the speciation process (e.g. Barraclough and Nee[2], this issue). Although it is inconvenient for some applications, the variability in timings can also be informative. Differences between loci can be used to draw inferences about the past population size and population subdivision. This approach will become more important as comparisons between species are more routinely made at multiple loci. The results could provide clues about the demography of populations that have undergone speciation.

Under the assumption that the ancestral species had a population size similar to the current species, it is possible to make a crude correction for the bias in timings that result from T_1. This makes use of the similarity between times to a common ancestor for the genes at a locus within a species and T_1 (Box 2). This and more sophisticated methods that deal with information from multiple loci are reviewed and developed by Edwards and Beerli[3].

Figure I in Box 1 provides a simplified view of speciation. There is a single point at which the inverted 'Y' splits, implicitly indicating that the ancestral species divided instantaneously into two descendant species between which there was no gene flow. Many of the modes of speciation sketched by Turelli *et al.*[4] (this issue) would involve a more protracted interruption of gene flow. Populations diverging in ALLOPATRY could sporadically come into contact, the accumulation of REPRODUCTIVE ISOLATION in SYMPATRY or PARAPATRY might

http://tree.trends.com 0169–5347/01/$ – see front matter PII: S0169-5347(01)02203-0