opmental processes which have occurred in the two masses of tissue." Waddington suggested that the terms epigenetic constitution or epigenotype be used to refer to the "set of organizers and organizing relations to which a certain piece of tissue will be subject during development." These terms in hand, he then urged that we consider "the appearance of a particular organ [as] the product of the genotype and the epigenotype, reacting with the external environment." Thus, in this manner, Waddington drew the original concept of epigenesis closer to those of genotype, phenotype, and development.

With regard to the quotation from Wright that Rubin mentions, I would also agree. We must keep in mind the context in which a gene works and that, as we broaden our understanding of the gene, the boundary of the gene might become less obvious. By way of thanks, I append a quotation from a paper published by H. J. Muller in 1938. Its focus, the phenomenon of position effect, differs from the issue addressed by Wright, but its flavor seems reminiscent of Wright's message.

> In the production of phaenotypic effects the gene must begin by interacting with cellular substances so as to produce a highly specific product or products, which must diffuse out from the locus of activity of the gene and in turn cause (or affect) further physiochemical changes. In the course of one of these chains of reaction, that has its origin in an individual gene, there will be many opportunities for interaction with other chains of reaction present in the complicated mixture; thus, the reactions will really form a kind of multi-dimensional net, rather than a simple chain. The final phaenotypic manifestations lie at the ends of the net furthest removed from the inner gene ends, and their quality depends upon the character and strength (including speed) of all the intermediate reactions and interactions (*3*, 1938, p. 588).

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4. I thank M. Green at the University of California, Davis, for alerting me to Waddington's 1939 discussion of epigentics.

Speciation and Centromere Evolution

A NEW MODEL FOR THE ORIGIN OF SPECIES IS proposed by S. Henikoff and co-authors in their review "The centromere paradox: Stable inheritance with rapidly evolving DNA" (special issue on Epigenetics, 10 Aug., p. 1098). Referring to the research in *Drosophila* to illustrate their idea, Henikoff *et al.* suggest that concerted evolution of centromeric satellite DNA and the centromeric histone protein centromere identifier (Cid) in isolated populations should result in a loss of compatibility between these elements in the hybrids. This should lead to chromosome nondisjunction (the failure of homologous chromosomes to segregate properly during meiosis) in the hybrids, and their sterility. Therefore, "speciation is an inevitable consequence of centromere evolution."

The authors suggest several tests for their model, but there is a simple test that should be definitive. If the model is correct, then the genes for hybrid sterility must be located predominantly at centromeres or the sites of Cids (or both). Alas, the mapping data from *Drosophila* and mouse indicate that they are not.

In formulating their model, the authors appear to have overestimated the role of chromosome nondisjunction in hybrid sterility. This type of malfunction of the chromosome segregation machinery accounts for only a minor part of gametogenic failure in hybrid animals. The major causes are the inability of hybrid germ cells to enter meiosis or to proceed through meiotic prophase. Another cause of hybrid sterility is the formation of nonfunctional gametes resulting from disruptions of the process of postmeiotic modifications (*1*). None of these events is associated with chromosome nondisjunction. Thus, apparently DNA satellite/Cid divergence takes place after the speciation event and is a consequence rather than a cause of speciation.

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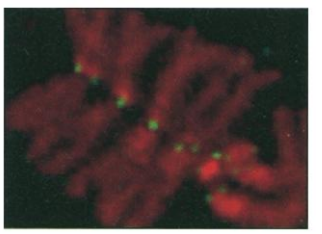
Response

BORODIN RAISES THE IMPORTANT ISSUE OF THE connection between hybrid sterility and sex chromosome nondisjunction that we discussed in our review. He points out that nondisjunction is not expected to result in spermatogenic failure. However, the actual situation is more complex. In *Drosophila,* nondisjunction of the *XY* pair caused by alterations in centromeric *X* heterochromatin is correlated with failure of sperm development (*1*), and failure occurs whether or not the *X* and *Y* chromosomes had been paired at meiotic prophase (*2*). To explain these puzzling observations, McKee and colleagues (*3*) have proposed the existence of a meiotic checkpoint that aborts spermatogenesis when proper orientation of the centromeres is not achieved. Metaphase checkpoints that monitor tension on spermatocyte kinetochores (the attachment point of microtubules to the centromere) are well known (*4*), and unequal pulling on *X* and *Y* centromeres should trigger such a checkpoint. The operation of an early checkpoint is consistent with postmeiotic defects, because failures in the early steps of meiosis can cause sperm dysfunction at much later stages of gamete development (*5*). Therefore, both nondisjunction and sperm dysfunction would result from unequal pulling on *X* and *Y* centromeres.



The centromeric protein Cid is revealed by antibody labeling (green) in these *Drosophila melanogaster* prometaphase chromosomes.

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Borodin also questions the agreement of our model with current mapping data. However, in established species, such as those cited by Borodin, mapping of a locus involved in an initial speciation event is complicated by the accumulation of complex secondary hybrid incompatibilities (*6*). These secondary incompatibilities would be indistinguishable from the primary one. To map primary speciation loci, one should use incipient species, such as the 150,000-year-old Bogotá population of *Drosophila pseudoobscura* (*6*). In this case, very few incompatibilities were detected. As Borodin suggests, we expect that an initial hybrid sterility determinant should map to the *cid* gene encoding the centromeric histone, or to another gene that alleviates unequal pulling on centromeres. Candidate proteins that might alleviate this imbalance include the *Drosophila* DNA binding protein

Prod, which binds to a species-specific satellite DNA during mitosis (*7*). Another is the protein encoded by the *Drosophila mauritiana* hybrid sterility gene, *Odysseus,* which might affect centromere imbalances by binding to satellite DNA through its adaptively evolving homeobox sequence (*8*). Because such proteins from one species will become incompatible with multiple centromeres from the other species, we do not necessarily expect that hybrid sterility will map to any particular centromere. Therefore, the simplest test of our model is the examination of Cid and other candidate proteins in incipient species.

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Tapping Science's Women for the Podium

ONE OF THE FINDINGS FROM THE SALARY AND job survey of life scientists conducted by the American Association for the Advancement of Science (publisher of *Science*) was that women scientists were less satisfied in their work than their male counterparts in a number of areas including job security, salary and compensation, promotion opportunities, and prestige ("General contentment masks gender gap in first AAAS Salary and Job Survey" by C. Holden, 12 Oct., p. 396).

For any scientist's career advancement, visibility is critical. A resource for meeting organizers that helps this issue for women biologists is the Speakers Resource Bureau (SRB) (accessed at www.ascb.org) established in 1997 by the Women in Cell Biology Committee of the American Society for Cell Biology. The SRB members are accomplished women scientists who have volunteered to provide advice to meeting organizers in selecting women speakers from a large number of different scientific fields, even beyond those usually considered to be in the area of cell biology, who are skilled at communicating about those disciplines. Through their knowledge about their senior and junior, U.S. and international women colleagues, SRB members provide a way for meeting organizers to tap the talents of many scientists who might otherwise have escaped notice. And for the speakers, such opportunities and visibility can contribute to greater job satisfaction.

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CORRECTIONS AND CLARIFICATIONS

PERSPECTIVES: "Where has all the carbon gone?" by S. C. Wofsy (22 Jun., p. 2261). The first sentence should have read, "Emission rates of CO_2 from combustion of fossil fuel have risen almost 40% in the past 20 years, but the annual increase in the atmosphere has stayed level, or even declined slightly." And the end of the last sentence of the figure legend on p. 2261 should have read, "...20 to 40% of U.S. fossil fuel emissions," not 20 to 40% of fossil fuel emissions worldwide.