Mezić *et al.* aim to find not just barriers but also regions that are particularly active in mixing the fluid. Such regions can lead, for instance, to a more rapid breakdown of oil into less harmful microdroplets. Their models rely on the concept of hyperbolicity of a flow: Hyperbolic flows are good at stretching fluid parcels. As the flow in the Gulf of Mexico is not periodic, and we have limited data, they introduce mesohyperbolicity: hyperbolicity on average. This reflects the fact that a typical fluid parcel may meet regions that are both favorable and adverse to mixing over a finite stretch of time. Mesohyperbolicity is a generalization to finite time of the concept of a Floquet analysis for periodic flows, where we can deduce the long-time behavior by examining a single period.

Mezić *et al.* were successful in describing how the oil was dispersed after the Deepwater Horizon oil leak. The oil spill occurred just as interest in these dynamical systems ideas is the subject of renewed interest. But hopefully we will be better prepared when another oil leak occurs, and applied mathematicians can work in conjunction with cleanup crews to predict where efforts are best focused.

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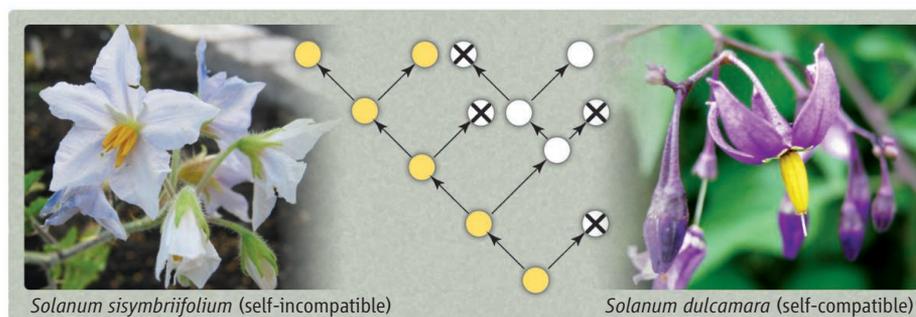
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## EVOLUTION

# The Long-Term Benefits of Self-Rejection

*A trait that prevents self-fertilization in plants appears to promote evolutionary diversification.*

Stephen I. Wright and Spencer C. H. Barrett

Charles Darwin provided the key explanation for the striking adaptive fit of organisms to their environments; traits that confer a greater chance of survival and reproduction spread through populations by the process of evolution by natural selection. But natural selection has no foresight; only immediate advantages matter. So the same trait that confers higher fitness in the short term could also increase the chance that a species eventually becomes extinct, or decrease the chance that it will form new species. Conversely, another trait may enhance a species' ability to diversify, leading to more species with that trait.

Many evolutionary biologists refer to such trait-specific effects on species diversification as "species selection," an evolutionary process that occurs above the species level (*1*). Biologists mostly accept the concept, but its general importance has not been clear. On page 493 of this issue, however, Goldberg *et al.* (*2*) provide a compelling case for the importance of species selection. In a study of hermaphroditic plants, in which individuals function as both males and females, they show that one trait——the ability of an individual to prevent self-fertilization by recognizing and rejecting its own pollen——appears to have strongly affected species diversification in the nightshade family, Solanaceae.

Hermaphroditic plants exhibit either self-compatibility (SC), which means an individual can act as both mother and father to its own offspring, or self-incompatibility (SI), which enforces outcrossing. SI is a genetically controlled physiological mechanism that is mediated by protein-protein interactions. It is analogous to a lock-and-key mechanism, in which the maternal parent recognizes pollen grains (or pollen tubes) that share alleles, initiating a biochemical pathway that rapidly blocks fertilization (*3*). The primary advantage of SI is that it avoids the harmful effects of inbreeding, particularly self-fertilization. However, SI comes at a cost because plants produce offspring that are just 50% related to them, rather than 100%, thus reducing transmission of their own genes to the next generation. Also, fertility can be severely compromised if pollinators or mates are unavailable. Because of these disadvantages, flowering plants have lost SI on numerous occasions during their evolutionary history, resulting in SC. Because of the complexity of SI, the trait is rarely, if ever, regained. This implies that SI may be on its way to extinction, yet at least half of all living flowering plant species are SI. Perhaps SI has some macroevolutionary advantage allowing it to be maintained by species selection.

Evaluating the importance of species selection is difficult, because it is tricky to estimate rates of character transition (such as a switch from SI to SC) separately from rates of speciation and extinction. Recent statistical advances, however, now allow researchers to analyze this question by using evolutionary trees (*4*, *5*). Using extensive phylogenetic information on species relationships in Solanaceae (which includes important crop plants, such as tomato, potato, and tobacco), the authors reconstructed the evolutionary history of transitions from SI to SC. They relied on well-resolved clades (groups of species



**Know thyself.** Species selection maintains self-incompatibility. Self-incompatible species (yellow circles) frequently experience evolutionary transitions to self-compatibility (white circles), leading to the potential loss of the trait over evolutionary time. This is balanced by a higher rate of extinction of self-compatible species (crosses), causing the stable maintenance of both types over long periods of evolutionary time.

*Solanum sisymbriifolium* (self-incompatible)   *Solanum dulcamara* (self-compatible)

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that share common ancestry). In this family, the evolutionary transition from SI to SC has occurred independently on numerous occasions. This is important because it improves statistical power and increases confidence that the transition itself is closely associated with differences in species diversification.

Goldberg *et al.* showed that SI lineages have a higher net diversification rate——a key quantity that determines the rate of increase in species numbers—than SC lineages. One key finding of their study is that this difference is not due to a higher rate of speciation for SI lineages; in fact, inferred speciation rates were higher in SC lineages. Instead, SC lineages have higher extinction rates than SI lineages. As a result, SI lineages have higher net diversification rates that apparently have been sufficient to counter-balance the repeated loss of the trait, allowing it to be maintained over evolutionary time (see the figure). The results provide a convincing macroevolutionary explanation for how SI has persisted over tens of millions of years despite its repeated breakdown to SC.

Given these results, a number of outstanding questions remain. Most importantly, why should SC plants that have the potential to self-fertilize experience higher rates of extinction? This study did not address the issue of how much "selfing" occurs in SC species, but the process is commonly associated with reduced

genetic diversity and lower rates of recombination. This reduces the chance of eliminating deleterious mutations and can decrease opportunities for adaptive mutations to succeed (*6*), both of which can increase the probability of extinction. Because some of the species included in the study probably self-fertilize at high rates, it is possible that the actual driver of differential diversification is not SI per se but the rate of self-fertilization. If the researchers had been able to use actual data on rates of cross- and self-fertilization (rather than only classifying plants as SC or SI), even stronger differences in diversification may have been found. However, obtaining this information for the many species included in this study would be a Herculean task.

Different approaches to studying the evolutionary consequences of selfing have provided conflicting results. Molecular work on protein evolution has found little evidence that selfing populations accumulate harmful mutations (*7*, *8*). In contrast, phylogenetic studies indicate that selfing species commonly produce short branches on evolutionary trees and appear to be more prone to extinction (*9*, *10*). One possible explanation is that molecular studies have focused on too coarse a level to detect the predicted differences in the efficacy of selection. New approaches that enable simultaneous estimates of the strength of positive and negative selection are likely to be

more powerful (*11*, *12*). Also, with few exceptions (*8*), molecular evolutionary studies have not been done with a large number of species, making it difficult to detect repeated declines in fitness of selfing lineages. Finally, SC lineages may experience higher extinction rates for reasons unrelated to mutational decay. For example, SI species often occur in relatively large, often long-lived, populations, and these demographic properties may make them more likely to persist over longer time scales. The causes of differences in diversification rates among lineages remain a central issue in evolutionary biology, but this illuminating study indicates that we should not ignore macroevolutionary processes in trying to understand the maintenance of adaptations and biodiversity.

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EPIDEMIOLOGY

# Environment and Disease Risks

Stephen M. Rappaport and Martyn T. Smith

*A new paradigm is needed to assess how a lifetime of exposure to environmental factors affects the risk of developing chronic diseases.*

Although the risks of developing chronic diseases are attributed to both genetic and environmental factors, 70 to 90% of disease risks are probably due to differences in environments (*1–3*). Yet, epidemiologists increasingly use genome-wide association studies (GWAS) to investigate diseases, while relying on questionnaires to characterize "environmental exposures." This is because GWAS represent the only approach for exploring the totality of any risk factor (genes, in this case) associated with disease prevalence. Moreover, the value of costly genetic information is diminished when inaccurate and imprecise environmental data lead to biased inferences regarding gene-environment interactions (*4*). A more comprehensive and quantitative view of environmental expo-

sure is needed if epidemiologists are to discover the major causes of chronic diseases.

An obstacle to identifying the most important environmental exposures is the fragmentation of epidemiological research along lines defined by different factors. When epidemiologists investigate environmental risks, they tend to concentrate on a particular category of exposures involving air and water pollution, occupation, diet and obesity, stress and behavior, or types of infection. This slicing of the disease pie along parochial lines leads to scientific separation and confuses the definition of "environmental exposures." In fact, all of these exposure categories can contribute to chronic diseases and should be investigated collectively rather than separately.

To develop a more cohesive view of environmental exposure, it is important to recognize that toxic effects are mediated through

chemicals that alter critical molecules, cells, and physiological processes inside the body. Thus, it would be reasonable to consider the "environment" as the body's internal chemical environment and "exposures" as the amounts of biologically active chemicals in this internal environment. Under this view, exposures are not restricted to chemicals (toxicants) entering the body from air, water, or food, for example, but also include chemicals produced by inflammation, oxidative stress, lipid peroxidation, infections, gut flora, and other natural processes (*5*, *6*) (see the figure). This internal chemical environment continually fluctuates during life due to changes in external and internal sources, aging, infections, life-style, stress, psychosocial factors, and preexisting diseases.

The term "exposome" refers to the totality of environmental exposures from conception onwards, and has been proposed to be a

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