Evolutionary biology

What do we know about speciation?

J.A. Coyne and N.H. Barton

ALTHOUGH darwinism is often declared to be dead, it refuses to lie down. Darwin did, however, mislead his audience in one way: his best-known work is much more about the origins of adaptations than of species. Since then, there has been much more progress in understanding the causes of adaptive change than of the mechanisms whereby new species are generated. In the past decade, attention has shifted back to the problem of how and why living creatures are organized into clusters of similar phenotypes. A perspective on this long-standing puzzle was provided at a recent meeting*.

Clustering can arise in several ways: interbreeding among sexually reproducing organisms; descent from a common ancestor; constraints on available genetic variation; or direct adaptation to environmental factors. These different pressures are reflected by diverse definitions of 'species'. The most widely accepted is the 'biological' species: a group of individuals characterized by heritable differences that prevent exchange of genes with related groups[1]. A.R. Templeton (Washington University, St Louis) argued that species definitions should instead be in terms of the processes which maintain the integrity of a cluster: he suggested defining "a group . . . whose range of variation is limited by genetically based cohesion mechanisms". As an alternative, J. Cracraft (University of Illinois, Chicago) put forward a 'phylogenetic' species concept, in which a species must include all individuals that share a common ancestor. All these definitions coincide where distinct groups coexist without interbreeding. But each is at least as difficult to apply to populations in different places as the traditional concept of the biological species. Both may split biological species into arbitrarily small units: taxonomy is hard enough without admitting this possibility.

What is the relation between reproductive isolation and morphological clustering? Although the two must usually be correlated, there is little support for the tenet of punctuated equilibrium, that substantial morphological change is permitted only by the simultaneous establishment of reproductive isolation[2]. Fully isolated species can be osteologically identical, so that speciation events may frequently be missed in the fossil record (A. Larson, Washington University, St Louis). Conversely, immense morphological change can occur without noticeable reproductive isolation, as in the allopatric races of the Hawaiian plant *Bidens* (F. Ganders, University of British Columbia). Although speciation is not required for morphological change, it can preserve it, because reproductive isolation can perpetuate local adaptations that would normally disappear with ecological change and gene flow (D. Futuyma, State University of New York, Stony Brook). This might yield an apparent correlation between speciation and punctuated morphological change.

There is still no disagreement with the dogma that speciation in sexual groups usually requires geographical isolation but occasional sympatric speciation (that is, speciation within one area) has not been excluded. A first step in this process, the development of polymorphism for resource use in a single population, was described for bluegill sunfish by D.S. Wilson (Kellogg Biological Station, Michigan) and for Galapagos finches by P. and B. Grant (Princeton University). It is also known in *Pyrenestes* finches from Africa[3]. The genetic basis of all these polymorphisms is unknown, however, and a crucial step — the evolution of assortative mating — has not occurred in the finches and is not yet known in sunfish. Partitioning of niches within a species is probably far more common than is sympatric speciation; indeed, the polymorphism of Galapagos finches completely disappeared with an ecological change on the island.

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Did the Hawaiian Drosophila *evolve through founder events, sexual selection or adaptive divergence? Left,* D.heteroneura*; right,* D. nigribasis. *(Courtesy of M.P. Kambysellis.)*

The factors that hinder sympatric speciation also cause problems for the evolution of reinforcement, the evolutionary increase of mating isolation which might occur when partially intersterile populations come into contact. This once popular concept lacks theoretical and empirical support: several other processes can produce heightened mate discrimination where species overlap, and evidence from narrow hybrid zones suggests that reinforcement is rare (R. Butlin, University College Cardiff). However, the observation that sympatric pairs of *Drosophila* species show much stronger assortative mating than do allopatric pairs of similar age is strong evidence of reinforcement (F. Ayala, University of California, Irvine; J.A. and A. Orr, University of Chicago). Theoretical models reveal many obstacles to reinforcement, but do not exclude it[4].

Hybrid zones can also reveal the ecological and demographic factors which influence interactions between divergent populations. Even within a group, hybrid zones can range from smooth intergradations with extensive hybridization to narrow overlaps containing few hybrids (for example, *Ensatina* salamanders, D. Wake; *Thomomys* pocket gophers, J. Patton and M. Smith, all at the University of California, Berkeley). In the alpine grasshopper *Podisma pedestris*, two chromosome races meet along a mountain ridge, and apparent anomalies in gene position can be accounted for by local density[5] (G. Hewitt, University of East Anglia). In contrast, the hybridizing crickets *Gryllus firmus* and *G. pennsylvanicus* are distributed in a mosaic across the eastern United States, in direct response to local soil type[6] (R.G. Harrison, Cornell University, New York).

Ecology and demography are also relevant to another area of current controversy: the importance of founder events in speciation. Much work has been stimulated by the dramatic radiation of the Hawaiian *Drosophila* (see figure), in which more than 800 species have evolved in the relatively short time since the archipelago was formed (K. Kaneshiro, University of Hawaii). Early theories stressed the importance of loss of genetic variability[7]. However, arguments that population bottlenecks would not by themselves cause strong isolation (N.H. B.), and the striking sexual dimorphism in these flies, have led to the suggestion that founder events trigger runaway coevolution of male traits with female preferences[8] (Kaneshiro). Other equally dramatic island radiations have, however, prompted straightforward adaptive explanations. D. Otte (Academy of Natural Sciences, Philadelphia) argued that the extremely diverse songs of Hawaiian tree crickets have evolved primarily by selection against overlap with neighbouring species. On the Galapagos, the selective pressures which have forced Darwin's finches into diverse feeding strategies can be identified (Grant and Grant). The problem is to disentangle the effects of population bottlenecks, sexual selection, and adaptation to novel physical and biotic circumstances in causing speciation — a task that may be

* *Speciation*, Academy of Natural Sciences, Philadelphia, 5–8 November 1987.

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insuperable.

Our understanding of speciation has progressed depressingly little since the classic reviews by Dobzhansky[1] and Mayr[9]. This is partly because of the difficulties of studying a historical process. But it also results from the preoccupation with schemes such as sympatric and chromosomal speciation, and speciation caused by genetic drift, that have little theoretical or empirical support and are considered infrequent even by their proponents. Like Wright's shifting balance theory, these processes may operate in nature and may even be demonstrable in the laboratory, but in nature are hard to distinguish from better-established alternatives.

Nevertheless, there are some questions that seem more tractable. How many genetic changes separate two species? Although there are straightforward methods for mapping genes causing reproductive or morphological differences, there have been comparatively few genetic analyses of closely related species. In most animals, reproductive isolation stems from changes at many genes, but speciation in plants may often involve very few loci[10]. Are there other differences between plant and animal speciation? The Hawaiian *Bidens* show that substantial adaptive divergence can occur without reproductive isolation, perhaps because of the compartmentalized development of plants. What is the normal function of genes that cause reproductive isolation? Mapping should soon permit cloning and sequencing, and provide clues to their normal role in development. More attention should be devoted to the possibility of speciation through sexual selection, where the connection between selection and reproductive isolation is clear. Are there 'rules' of speciation that apply across groups? The ubiquity of Haldane's rule in animals (the preferential sterility of heterogametic hybrids) and its likely origin by rapid evolution of the sex chromosomes[11] are two patterns without widely accepted evolutionary explanations. Comparative studies may reveal other such patterns and underscore the need for good systematics and accurate estimates of divergence times. A combination of genetic and developmental approaches may offer the most progress in understanding the evolution of reproductive isolation. Without such knowledge, we are simply unable to evaluate the many theories of speciation. □

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Vaccine development

Which way for malaria?

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THE discovery, recently reported[1] by Louis Schofield and collaborators, that immunity against malaria operates against stages of the parasite developing in the liver calls for a radical reappraisal of the ways in which malaria vaccines are being developed, and at the same time explains several paradoxes.

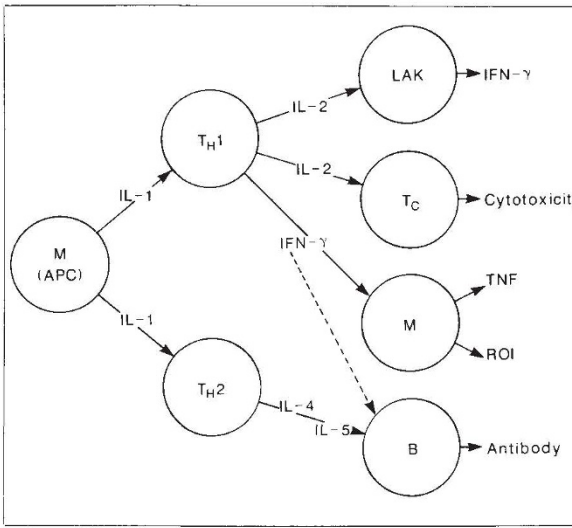
The life-cycle of the malaria parasite begins when a mosquito injects infective stages, called sporozoites, directly into a blood capillary. Sporozites enter liver hepatocytes within minutes and undergo a massive phase of asexual multiplication that results in the formation and release of up to 30,000 merozoites. These invade red blood cells and undergo further cycles of multiplication, destroying increasing numbers of erythrocytes. Sporozoites, liver-stages, merozoites and intraerythrocytic stages of the malaria parasite possess largely unique repertoires of antigens and, although clinical immunity is associated with the blood stages, the sporozoite is the obvious target for a vaccine.

Attempts to develop vaccines against sporozoites and blood stages have concentrated on the identification and synthesis of dominant surface proteins[2], but despite showing initial promise, this approach has been largely disappointing. Recombinant or synthetic sporozoite antigens protect some but not all of the volunteers[3,4], and the immunization of owl monkeys with a major blood-stage antigen of the malaria parasite *Plasmodium falciparum* was only partially effective[5].

There are some reservations about sporozoite and blood-stage vaccines. The main arguments against a sporozoite vaccine are that only one sporozoite needs to escape to the liver to initiate an infection, and that in endemic areas people acquire high levels of anti-sporozoite antibodies but still become infected. An argument against merozoite or blood-stage vaccines is that although they might ameliorate clinical disease, they cannot prevent infection. The liver stages of the parasite have received relatively little attention because it has been widely believed that no immunity to these intracellular forms exists. The recent work by Schofield *et al.*[1] shows this assumption to be false, and also points to the central involvement of antibody-independent immune mechanisms in immunity to malaria.

Development of the liver stages of *P. berghei*, a malaria parasite of rodents, can be prevented *in vivo*[6] and *in vitro*[7] by administration of minute quantities of gamma-interferon (IFN-γ) — but if this is a transient phenomenon it is unlikely to be of any practical importance. Schofield *et al.*, also using *P. berghei*, treated rats immunized with attenuated sporozoites, a very effective method of vaccination, with a monoclonal antibody capable of neutralizing IFN-γ. This treatment not only permits infection of liver cells but also reverses established sterile immunity. The protective effect of IFN-γ is therefore not transient, but is an integral part of the immune response to malaria.

Several points concerning vaccination emerge from these experiments. Protective vaccination can be achieved by



Part of the immunoregulatory circuit. Parasite antigens are processed by macrophages (M) which act as antigen-presenting cells (APC). The first signal is interleukin-1 which activates two kinds of helper T-cells (T_H1 and T_H2). Further signals such as interleukin-2 (IL-2) activate lymphokine-activated killer cells (LAK) or cytotoxic T-cells while gamma-interferon (IFN-γ) activates further macrophages, and interleukins 4 and 5 (IL-4 and IL-5) activate B-cells. The net result is the production of cytotoxic T-cells, antibody, IFN-γ, tumour necrosis factor (TNF) and reactive oxygen intermediates (ROI), which separately or together can destroy malaria parasites. Interferons can also inhibit B-cell activity (broken line).

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