a relatively long breeding lifespan but, as yet, we do not know whether such factors are heritable or whether contingency is largely responsible. This will be a major challenge for studies of seabirds in the future.

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Marine Speciation on a Small Planet

Stephen R. Palumbi

The scale of population structure in many marine species is on the order of thousands to tens of thousands of kilometers. How does speciation take place in oceans that are only about this same size? Recent results suggest an important role for transient isolation, gamete ecology and molecular evolution at gamete recognition loci. These factors have long been appreciated by plant biologists, and are likely to be a fruitful area of research for marine biologists as well.

Despite the central place of speciation theory in evolutionary biology, there is a great deal of uncertainty and controversy about how speciation occurs[1,2]. This is partly because most proposed speciation mechanisms are at least theoretically possible[2], and because case studies of speciation in one group (e.g. the Hawaiian *Drosophila*) may not apply to other taxa with different life histories, morphologies or ecologies[2,3]. Some of the most extreme differences in life histories occur between behaviorally complex taxa with low dispersal, such as many insects and vertebrates, and high-dispersal taxa showing limited adult mating behavior, such as plants or many marine invertebrates.

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Dispersal, mating systems and speciation

Because population structure and genetic divergence are tightly coupled, species with very different life history strategies are likely to speciate in very different ways. Most of the attention of evolutionary biologists has been directed towards divergence in terrestrial or freshwater animals with relatively small population sizes, narrow ranges, low dispersal or low fecundity[4]. In these cases, models of selection and gene flow often correspond reasonably well with the patterns of divergence observed among natural populations. Dispersal is sometimes low enough so that gene introgression through hybrid zones can be mapped and studied in great detail[5]. Even birds seem to fit these expectations fairly well, despite their potentially higher dispersal capability[6].

Taxa with high dispersal and high fecundity often show a very different pattern. In terrestrial systems, seed plants have some of the highest fecundities and potential dispersal distances known. Patterns of speciation in plants are very different from those in terrestrial animals[7]. In plants, sympatric sister species

sometimes differ by only a few small genetic changes[8], and often show widespread hybridization[9]. Increasingly, attention has focused on how mating systems evolve between plant populations[10], and how barriers to gene flow develop by inbreeding within local demes[11]. Because of this, many plant species seem to fit the 'recognition' species concept of Patterson[12] rather than the 'isolation' species concept typical for terrestrial animals[4].

The distinctions between low-dispersal animals and high-dispersal plants are beginning to channel thinking in evolutionary biology in interesting ways[8,9]. However, a third category of species continues to receive very little attention. High-dispersal animal species are rare on land, but make up the dominant component of the marine fauna. Such species have free-swimming adults or planktonic larvae that can drift for hundreds or thousands of kilometers before metamorphosing into adults. Typically, ranges are vast, populations are large, and fecundities number in the millions of eggs per female.

Carson[9] advocated a unification of speciation models to explain patterns in high-dispersal plants and low-dispersal animals. Will such models also explain speciation patterns in high-dispersal animals? Are speciation patterns more similar between plants and marine animals because of their similar life histories, or between marine and terrestrial animals because of their phylogenetic history? The latter possibility seems likely, mainly because high-dispersal marine animals and their low-dispersal terrestrial counterparts still share important properties not shared with plants. Yet, new information about sister species in marine systems shows strong parallels to patterns of plant speciation.

Table 1. Genetic structure and dispersal in marine species

Organisms	Dispersal	Method[a]	Differences among demes	Geographic scale (km)	Refs
Gastropods					
(*Nucella*)	Low	Protein	High	200	29
(*Littorina*)	Low	Protein	High	1	30
(*Littorina*)	Low	Protein	High	1	31
Fish					
catfish (*Arius* and *Bagre*)	Low	MtDNA	None	1500	32
toadfish (*Opsantus*)	Low	MtDNA	High	100	32
Copepods (*Tigriopus*)	Low	Protein	High	2	33
Horseshoe crabs					
(*Limulus*)	Low	Protein	High	3000	34
(*Limulus*)	Low	MtDNA	High	3000	35
Urchins					
(*Strongylocentrotus*)	High	ScnDNA	None	2000	36
(*Strongylocentrotus*)	High	MtDNA	None	1500	18
(*Strongylocentrotus*)	High	MtDNA	None	15000	19
(*Arbacia*)	High	Protein	High	1000	37
Mussels					
(*Mytilus edulis*)	High	Protein	High	2000	38
(*M. edulis*)	High	Protein	High	40	15
(*M. californianus*)	High	Protein	Slight	4000	39
Fish					
reef fish, 12 spp.	High	Protein	Slight	5000	40
milkfish (*Chanos*)	High	Protein	Slight	10000	41
eels (*Anguilla*)	High	MtDNA	None	3000	42
Oysters (2 genera)	High	Protein	Slight	2000–3000	43
(*Crassostrea*)	High	MtDNA	High	100	16
Gastropods					
(*Littorina*)	High	Protein	Slight	1000	30,31
(*Nassarius*)	High	Protein	None	1000	44
Lobsters (*Homarus*)	High	Protein	Moderate	1000	45
Whales (*Megaptera*)	High	MtDNA	High	3000	17

[a] MtDNA, mitochondrial DNA; ScnDNA, single-copy nuclear DNA.

Speciation in the sea

Generalizations about speciation mechanisms between plants and animals, or between terrestrial and marine habitats, are very incomplete because information about speciation in the sea is only beginning to emerge. In marine systems, the best information has been on speciation among taxa with life histories similar to terrestrial species: those with low dispersal and small population sizes. A large number of studies have shown that species with low dispersal tend to have significant genetic structure over small spatial scales (Table 1), show physiological adaptation to local conditions, and have high rates of speciation[13]. These patterns are not dramatically different from those in terrestrial and freshwater habitats.

Speciation in high-dispersal taxa is much more poorly understood. Yet these groups provide the greatest challenge to the common evolutionary paradigm of slow species divergence in allopatry. In general, high-dispersal taxa have large population sizes, huge ranges and rapid gene flow: characteristics that should slow species formation. Protein electrophoresis has shown that genetic differences among localities tend to be slight in species with larvae that have long residence times in the plankton (Table 1). The fossil record confirms that species with high larval dispersal have broader geographic ranges, greater species durations, and slower rates of speciation than similar species with low dispersal[13]. These studies support the early generalization that speciation in the sea is usually by gradual build-up of genomic incompatibility in allopatric populations, and that such genetic divergence of high-dispersal populations is minor and slow[14].

Yet, species richness in marine environments is often exceptionally high. The Indo-Pacific has one of the highest densities of species known, with thousands of sympatric species of fish, corals, crustacea, algae and other taxa[3]. Either these species are ancient products of slow speciation[14], or the slow, allopatric paradigm is incomplete.

To date, several possible qualifications to standard speciation models are known. First, high dispersal potential does not always lead to high gene flow because of selection[15], local genetic drift[16] or complex homing behavior[17]. Second, isolation by large distances allows for genetic divergence even in high-dispersal species. In general, distances in excess of thousands of kilometers are required. Our studies of mitochondrial DNA variation in sea urchins show no genetic differences in *Strongylocentrotus purpuratus* over 2500 km along the west coast of North America, but slight differences

occur in *S. droebachiensis* between the Atlantic and Pacific Oceans[18]. For *S. pallidus*, the most common mitochondrial genotype is indistinguishable between Pacific and Atlantic Oceans, but some ocean-specific genotypes exist[19]. In the tropical Pacific, isolated archipelagoes have lower mtDNA diversity than islands in the western Pacific[20], but the same mtDNA genotypes are shared over 10 000 km.

Genetic structure may also be initiated by extrinsic geological factors. Springer[21] proposed that tropical blennies were divided into western and eastern sister species by the movement of the subcontinent of India from Madagascar to its current position in Asia over the past 65 million years. In addition, the existence of a suite of tropical marine invertebrate species whose distributions are limited to the Pacific tectonic plate[3] suggests that species distribution patterns are determined by movement of these plates through geological time.

Thus, there is a range of mechanisms (selection, distance, geology, behavior) that can lead to genetic structure in high-dispersal species. However, these mechanisms do not explain how reproductive isolation evolves in the divergent populations. Because the extrinsic isolating mechanisms described above act on large geographic scales (except perhaps behavior), the isolated populations will most often be large[14]. How does reproductive isolation develop between two large gene pools? Mayr[14] proposed that slow allopatric genetic divergence occurring over tens of millions of years accounts for patterns of speciation in sea urchins.

Despite these predictions of slow divergence, the appearance of new marine species in the fossil record can be abrupt, even in high-dispersal taxa. In order to investigate the mode of speciation in gastropods, Jablonski[13] recorded where (geographically) each fossil species in the collection first occurred in relation to its nearest relative species. For taxa with high dispersal, species do not appear as if they evolved allopatrically from their nearest relatives, but rather 'appear randomly with respect to their closest relatives' geographic ranges'. This pattern needs explanation, and is difficult to reconcile with the view that high-dispersal species diverge gradually in allopatry.

Genetics and marine speciation

Further conflicting evidence for slow divergence can be found in genetic analyses of closely related marine species. Some marine genera have split into multiple species that show little genetic divergence. Urchins in the genus *Echinometra* are widely distributed in shallow reef environments across the tropical Pacific and Indian Oceans. They have typical larvae that spend 4–6 weeks in the plankton[20] and thus have high dispersal potential. Morphological work on adults and larvae shows the presence of four closely related, often sympatric species. Co-occurring species spawn eggs and sperm into the water at the same time, so few ecological barriers to reproduction between species are apparent.

Differences in mtDNA and single-copy nuclear DNA between the four species suggest recent speciation. Single-copy nuclear differences, based on thermal renaturation kinetics, are small, ranging from 1% to 3% (corrected for intraspecific variation). MtDNA divergence based on restriction-site changes[20] and cytochrome oxidase I gene sequences are also slight, ranging from 1% to 3% nucleotide substitutions. Such values suggest that these species arose in the Pleistocene. How did speciation occur? What maintains genetic boundaries among sympatric species?

Even though these species appear to be of recent origin, there is strong reproductive isolation between them. The strongest, most effective barrier is failure of sperm and eggs from different species to bind and fuse. Individuals with the same mitochondrial genotype and the same morphological features always produced more than 95% fertilized eggs, even though they might have come from 10 000 km apart (Okinawa versus Tahiti). Dissimilar individuals produced very few fertilized eggs, usually less than 1%, even when collected from the same tide pools[20]. Post-zygotic barriers to interspecific hybridization do not seem to be strong. The small percentage of eggs that are fertilized in interspecific crosses develop normally, showing only slight asymmetries in the larval skeleton. Hybrids can be raised to metamorphosis in the laboratory (T. Uehara, pers. commun.), and adults that are morphologically intermediate between species can be found (albeit rarely) in the field.

Because fertilization is well understood in sea urchins, we have been able to localize at least one of the systems that fails in *Echinometra* hybrid crosses. Fertilization consists of: (1) sperm approach, (2) the acrosome reaction, (3) penetration of the jelly coat, (4) attachment to and penetration of the vitelline membrane, and (5) plasma membrane fusion (Fig. 1). *In vitro* manipulations show that fertilization failure is not at steps 1–3 (Ref. 22). Furthermore, the intracellular electric potential of eggs shows no change in the presence of heterologous sperm (S.R. Palumbi and R. Kane, unpublished), strongly suggesting that the failure of fertilization occurs before step 5. To verify a fertilization block at step 4, we examined early fertilization by transmission electron micrography, and showed that sperm failed to attach strongly to the vitelline layer of heterospecific eggs (E.C. Metz, H. Yanagimachi and S.R. Palumbi, unpublished). Those sperm that did attach did not penetrate the vitelline layer to the egg membrane underneath. Thus, interaction of the sperm and the vitelline layer (step 4) is a primary site of fertilization failure.

Molecular biology of gamete interactions

These results implicate the interaction of gametes as a crucial stage in the development of reproductive isolation among these sea urchins. Sperm attachment in sea urchins is mediated by a sperm protein named bindin and a glycoprotein receptor on the egg surface[23]. Amino acid sequence differences between bindin proteins in different species are associated with fertilization failure, although a direct relationship between bindin evolution and reproductive isolation has yet to be shown. In *Echinometra*, amino acid differences in bindins

between species are far in excess of those predicted by single-copy renaturation results[22]. Because silent substitutions are no more common than predicted by the renaturation results, functional evolution in bindin appears to be occurring at a rapid rate.

Similarly, Vacquier *et al.*[24] have shown that interspecific crosses among different species of abalones (marine gastropods) fail because of failure of sperm to penetrate eggs of other species. The protein responsible for egg entry, lysin, has been sequenced for seven species and shows far more amino acid differences than silent substitutions between species (V.D. Vacquier, pers. commun.). Egg–sperm interactions appear to be evolving rapidly in abalones as well as urchins.

The implication of these results for urchins and abalones is that the interaction of a small number of gene products on the surfaces of eggs and sperm may play a disproportionate role in reproductive isolation of free-spawning marine invertebrates. Speciation and molecular evolution at these loci may be linked in tempo and mode.

Speciation and the ecology of sex

The erection of genetic barriers at the level of gamete interactions in marine animals is strikingly similar to the isolating mechanisms of many plants[10]. In many closely related plant species, cross-hybridization in the field appears to be limited by pollen–style interactions that inhibit the initiation of pollen tube growth[10], or slow it considerably. Such barriers between populations appear to be pleiotropic effects of genetic systems whose real function is to limit selfing. In some plants, both selfing and interspecific compatibility are controlled by an S-gene complex that 'controls breeding behavior and is believed to have hundreds of alleles'[10]. New alleles at the S loci may arise as a result of recombination during inbreeding of small isolated populations[25].

The similarity of isolating mechanisms between high-dispersal plants and marine animals parallels similarity in the ecology of reproduction. In both groups, adults are largely sedentary compared with the mobility of gametes, pollen or zygotes. Behavioral interactions between reproducing adults are largely limited to a few environmental or chemical cues before gametes are released into the habitat. As a result, egg–sperm or pollen–style interactions such as sperm chemotaxis[26] or pollen tube inhibition[10] assume greater significance than in behaviorally complex groups with elaborate mating signals. Dispersal is often passive, and occurs during an early developmental phase when the zygote has little or no capacity to control its motion. In addition, reproductive strategies such as selfing and vegetative propagation occur widely in plants and marine invertebrates, but are largely absent in terrestrial animals.

Of course, major differences exist in reproduction between marine animals and high-dispersal plants. Free-spawning animals have no ability to abort embryos selectively, as is so common among plants. Nor is there double fertilization or the interaction between maternal, zygotic and endosperm tissue as in plants. Many invertebrate larvae can behaviorally alter dispersal or settlement patterns[27], whereas few such options are open to plant seeds or spores. Perhaps most importantly, gamete interactions appear to favour closely related individuals in animals, but to favour outcrossing in plants.

What role does gamete incompatibility play in the speciation process? Very little information is available to answer this question for animals or plants. Pandey hypothesized that recombination during inbreeding gives rise to the large number of S-complex alleles in many plants[25]. Multiple bindin alleles have been discovered within urchin species (S.R. Palumbi, unpublished), although compatibility groups like those that exist in plant populations have yet to be discovered. Multiple bindin alleles must interact with gene products on egg surfaces that recognize them. Perhaps this interaction results in rapid coevolution of gamete recognition systems in males and females, similar to the rapid evolution possible in male and female sexual traits due to sexual selection[28]. This process may occur more quickly in partially isolated populations than the slow divergence typically invoked in allopatric speciation, and may occasionally result in populations that are isolated primarily by this mechanism. Currently, no population genetic models exist that adequately consider the coevolution of male and female gamete recognition loci in the context of speciation. Nor do we understand the degree to which rare mutants are at a reproductive disadvantage in natural populations. Third, the nature of selective forces acting on gamete recognition loci are undetermined. All these areas of research are central to understanding gamete ecology and speciation, and promise interesting insights in the future.

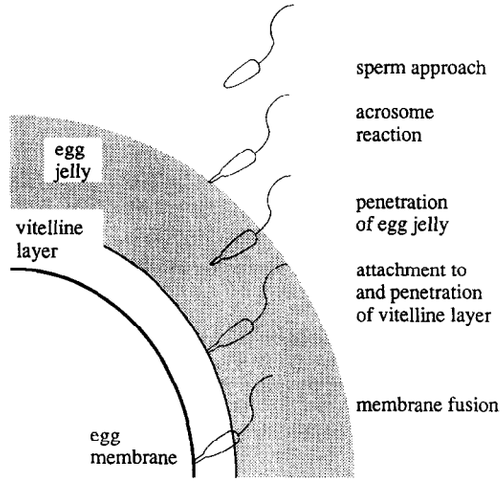

Fig. 1. Five stages of fertilization in free-spawning sea urchins. There is the possibility of species-specific egg–sperm interactions at all five stages, although for the genus *Echinometra*, only stage 4 has been implicated in reproductive isolation. Other animals have slightly different stages, but some type of egg–sperm interaction is universal.

Conclusions

Research on marine speciation remains in its infancy, but is accelerating because of the application of genetic tools in molecular biology to questions about population structure and the genetics of sister species. In general, speciation in high-dispersal marine species may depend on the evolution of gamete interactions and mating systems, as well as local adaptation and widespread genome incompatibility of allopatric populations. Although comparisons among such widely divergent groups as marine animals, plants and terrestrial animals are fraught with pitfalls, such comparisons may allow valuable insight into the relationships between dispersal, speciation and the ecology of sexual reproduction.

Lessons from the large literature on plant reproductive biology have already shown surprising parallels in marine systems, and will be a productive guide to future research.

Acknowledgements

I thank Ed Metz, Vic Vacquier and my parents for discussion about gametes, and Andrew Martin, Craig Moritz, Hampton Carson, Richard Strathmann and Mike Hadfield for comments on the manuscript. Supported by grants from NSF and the Whitehall Foundation.

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What is a Quasispecies?

Martin A. Nowak

A quasispecies is a well-defined distribution of mutants that is generated by a mutation–selection process. Selection does not act on a single mutant but on the quasispecies as a whole. Experimental systems have been designed to study quasispecies evolution under laboratory conditions. More recently, virus populations have been called quasispecies to indicate their extensive genetic heterogeneity. The most prominent examples are probably the human immunodeficiency viruses HIV-1 *and* HIV-2. *The quasispecies nature of* HIV *has formed the basis of a model that provides a mechanism for the pathogenesis of acquired immunodeficiency syndrome* (AIDS) *in humans. This article focuses on the nature of the quasispecies concept and its implications for evolutionary biology and virology.*

The term 'quasispecies' was introduced by Eigen and Schuster[1] in 1977, in the context of their work on the origin of life, to describe the cluster of closely related molecular 'species' produced by errors in the self replication of macromolecules (nucleic acids). This followed Eigen's first theoretical model of molecular evolution based on chemical kinetics[2].

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In the original notion of Eigen and Schuster, a quasispecies is defined as the equilibrium mutant distribution that is generated by a specific mutation–selection process describing the erroneous replication of macromolecules (nucleic acids)[1–7]. Suppose there are n different nucleic acid sequences I_1, I_2, ..., I_n that can serve as templates for replication. Each variant is characterized by a specific nucleotide sequence. This nucleotide sequence may determine the replication rate of a given variant. The replication rates of the variants I_1, I_2, ..., I_n may be denoted by a_1, a_2, ..., a_n. These quantities represent the selective values of the individual mutants. In the absence of mutation, the variant with the highest replication rate will grow fastest and reach fixation.

The result of selection in this world without errors is a homogeneous population consisting of the fastest replicating variant. But replication is not error free. Thus it is necessary to define the probabilities Q_{ij} that (erroneous) replication of template I_j results in the production of the sequence I_i. The quantities Q_{ij} for $i=1, 2, ..., n$ and $j=1, 2, ..., n$ form the so-called mutation matrix.

A system of ordinary differential equations describes the time evolution of the population of these nucleic acid sequences. The growth rate of a specific variant, e.g. I_1, can be written as

$$dx_1/dt = a_1Q_{11}x_1 + a_2Q_{12}x_2 + ... + a_nQ_{1n}x_n \quad (1)$$

Here x_1, x_2, ..., x_n denote the population sizes of the variants I_1, I_2, ..., I_n.