

## Population Genetic Structure and the Fixation of Chromosomal Rearrangements in *Sceloporus grammicus* (Sauria, Iguanidae): A Computer Simulation Study

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**This paper reports on a series of computer simulations designed to examine some population genetic correlates associated with the stochastic fixation of novel chromosomal rearrangements appearing in small isolated populations as specified by the cascading speciation model. Simulated populations were subjected to repeated bottleneck events for 100 breeding periods, with electrophoretic data being input from allele frequencies published for the chromosomally polytypic lizard *Sceloporus grammicus* (the complex for which the cascade model was formulated). These data were used to calculate several population genetic correlates over the duration of the simulations. When bottleneck sizes consisted of five individuals, extinction rates were high, but 1-2.5% of the populations survived and fixed new chromosomal rearrangements. The electrophoretic profile for this population structure reflected  $D$  and  $F_{IS}$  values nearly an order of magnitude higher than those calculated from natural populations. As founder populations are increased to 10 and 20 individuals, extinction rates decline, as do probabilities for fixing the novel rearrangements.  $D$  and  $F_{IS}$  values approximate those characteristic of natural populations of *S. grammicus* for founder populations of 20 animals.  $F_{ST}$  values remain high through all simulations. Within the constraints of the model, the cascading chromosomal speciation hypothesis proposed to explain the karyotypic diversity within *S. grammicus* appears unlikely.**

**R**ECENT reviews of the factors responsible for the fixation of new chromosomal rearrangements in natural populations, and the evolutionary consequences of such events, have shown that there are still many unknown variables that must be addressed empirically before we can clarify the role of chromosomal change in evolution (Patton and Sherwood, 1983; Baker et al., 1987; Sites and Moritz, 1987). One hypothesis that is exceptionally explicit in its assumptions and predictions is the cascading or chain process model of chromosomal speciation (Hall, 1983).

This model was based on a large cytogenetic data set for several genera of the geologically recent sceloporine lizard radiation, primarily to explain the high species diversity and chromosomal variability (range of  $2n = 22-46$ ) within the most derived genus *Sceloporus*, relative to several more ancestral, chromosomally monotypic and species-poor genera (Paull et al., 1976; Hall, 1980, 1983). The model also seeks to explain the extreme degree of chromosomal polytypy ( $2n = 32-46$ ) within what is currently recognized taxonomically as a single or at most two species, *Sceloporus grammicus* (Porter and Sites,

1986; Sites et al., 1987, 1988). Both Hall (1980, 1983) and White (1978) have previously considered this complex as exemplifying chromosomal speciation in progress.

Hall's model makes explicit assumptions about patterns of meiotic assortment in chromosomal heterozygotes from hybrid zones (strong underdominance), and also required population structure for *S. grammicus* (extremely subdivided). A strongly subdivided population structure is required if chromosomal rearrangements are strongly underdominant (selected against) as heterozygotes, because only in very small, isolated populations will sampling error have any reasonable chance of fixing such a rearrangement (Wright, 1941; Lande, 1979; Templeton, 1980). Consequently, Hall's hypothesis can be evaluated from both cytogenetic and population genetic perspectives.

Meiotic data are at present limited largely to analyses of intrapopulation polymorphisms in males (Hall, 1973; Porter and Sites, 1985, 1987), and the single hybrid zone studied to date yielded equivocal evidence for restricted gene flow between hybridizing cytotypes (Hall and Selander, 1973; Hall, 1980; Futuyma and Mayer,

1980) and did not include collection of meiotic data. We have attempted to indirectly evaluate the population genetic structure of selected geographic regions of the *S. grammicus* complex by electrophoretic studies (Sites and Greenbaum, 1983) and by comparison with a chromosomally monotypic congener, *S. graciosus* (Thompson and Sites, 1986). Our results generally suggest that *S. grammicus* may not have the population subdivision necessary to permit a reasonable chance of fixing strongly negatively heterotic chromosomal rearrangements. These empirical comparisons have been useful and informative, but interpretations must be made cautiously because of a number of unknown variables. For example, the age and number of speciation events leading to the lineages of *S. grammicus* and *S. graciosus* are unknown, as are influences of Pleistocene/post-Pleistocene vicariant events on the geographic structure of each. Without explicitly identical histories, there are any number of reasons why these two lineages might have similar or dissimilar patterns of intra- and interpopulation allelic diversity.

In the absence of data on the mating system, population biology, and dispersal patterns in *S. grammicus*, the consequences of the cascading speciation assumptions can be evaluated by appropriate computer simulation studies of the probability of fixing a negatively heterotic mutation for a variety of population sizes, migration rates, and relative fitnesses of the three possible genotypes for a single chromosomal rearrangement (AA, AB, BB). A number of analytical mathematical models (Hedrick, 1981; Slatkin, 1981; Walsh, 1982) and simulation studies address these issues in general terms (Bengtsson and Bodmer, 1976), and a few treatments address specific types of chromosomal changes (Lande, 1984, 1985) or founder events (Hedrick and Levin, 1984), but all show without exception that the stronger the selection against the chromosomal heterozygote, the more restrictive the population conditions must be to achieve fixation (Bengtsson, 1986). Once a new chromosomal rearrangement has become fixed in a single breeding unit, it can be spread to others with periodic extinction and recolonization of other demes. The probability of the eventual spread and fixation in a species of such a rearrangement is roughly equal to the probability of its fixation within a single deme (Lande, 1979).

In this paper we report on a series of com-

puter studies designed to simulate extinction/recolonization events, and generate a population genetic signature (Templeton 1980, 1981, 1982) for a series of hypothetical populations of *S. grammicus* of varying founder sizes, and under a range of selection coefficients against chromosomal heterozygotes. As pointed out by Lacy (1987), computer simulations share with analytical approaches the fact that both depend upon necessarily incomplete representations of natural processes (simplifying assumptions, omission of some factors, etc.). Yet, for studying the effects of variables that can be well defined, and for evaluating interactions among those variables, simulations may provide insights that are not intuitively obvious or obtainable by mathematical analysis. We have used a modified version of the model described by Chesser and Baker (1986) to include relevant ecological variables such as litter size, age-dependent mortality, generation time, etc., known or inferred for *S. grammicus*. The novel feature of this study is the inclusion of calculations for values of several population genetic correlates (Sites and Moritz, 1987) associated with populations structured to permit the fixation of new chromosomal rearrangements. The computer-generated set of population genetic correlates, based on real allozyme data incorporated into the simulations, is intended to serve as a sort of "null model" and guide interpretations of population structure from empirical data sets.

#### METHODS

*Simulations.*—The model allowed variable input of initial population size, number of offspring per female in each breeding period, fecundity reduction for chromosomally heterozygous individuals (selection against the rearrangement), number of founding populations, number of loci, initial electromorph (maximum of five) frequencies for each locus, maximum age, and age-specific mortality probabilities. Enzyme loci were assumed to be unlinked to each other or to the chromosomal rearrangement. Ages of individuals in a population represented their respective breeding periods. The model randomly designated the sex and genotypes (in accordance with input allele frequencies) to the founders of the initial populations. Each population was assigned a single chromosomal mutant, in a heterozygous condition, to a randomly selected individual. Mates were randomly selected within each population, and inbreeding was neither

promoted nor avoided. Reduction in the number of offspring for a mating was possibly only by way of fertility reductions imposed for individuals heterozygous for the chromosomal rearrangement. The populations were allowed to grow until a maximum population size was attained; subsequently, the population was bottlenecked by randomly selecting from the population the same number of individuals as in the original founding populations. Hall (1983) hypothesized that demes which have fixed one or more novel rearrangements are more likely to perpetuate the conditions favorable to the fixation of subsequent rearrangements, and it is this "selective founder effect" that is assumed to have produced the linear cascade of the cytotypes of *S. grammicus*. The multiple bottleneck procedure was repeated for 100 breeding periods or until the populations became extinct. Two hundred replicates of each set of conditions were analyzed.

Statistics calculated from each breeding generation were written to external files for subsequent analyses. These statistics included: a) the  $F_{ST}$  and  $F_{IS}$  coefficients (Wright, 1951, 1965; Nei, 1977); b) the average Nei's (1972) genetic distance (D) between populations; c) the D value for a population from one generation to the next; and d) extinction and fixation events. Genetic distance was the original population genetic correlate described by Templeton (1980) as possibly being useful for making inferences about some mechanisms of speciation. Given an adequate level of allelic variability in the ancestral population (Templeton et al., 1981), between population D values are predicted to be positively correlated with the degree of population subdivision, and hence the probability of fixing a strongly underdominant chromosomal rearrangement. The two F coefficients were not discussed in Templeton's original paper, but were qualitatively evaluated by Sites and Moritz (1987) in their review of genetic correlates of population structures associated with various modes of chromosomal speciation. The  $F_{ST}$  coefficient measures the degree of differentiation among subpopulations and can range in value from 0 (complete panmixia) to 1 (complete fixation of alternate alleles at all loci in different subpopulations).  $F_{IS}$  is an inbreeding coefficient and gives the probability that two alleles uniting to form a zygote in a breeding unit are identical by descent (i.e., were replicated from a single allele in an ancestor). Such a probability is measured relative to the total pool of alleles (for the

locus in question) available within the breeding unit (Hartl, 1980). It can also be thought of as a fixation index that can be parameterized to take on negative values and used to measure deviation from Hardy-Weinberg proportions within subpopulations, with positive values indicating a deficiency of heterozygotes, a zero value for random mating, and a negative value indicating heterozygote excess (Hedrick, 1983). When a subpopulation is closed to migration and consists entirely of a single breeding unit, as specified in our model, a positive  $F_{IS}$  value reflects inbreeding within the subpopulation. All data from these files were analyzed using programs from the Statistical Analysis System (SAS Institute Inc., 1985).

*Biological Parameters.*—Electromorph frequencies for the initial populations in the model were taken from 15 polymorphic loci screened in 13 populations of *S. grammicus* by Sites and Greenbaum (1983). The number of electromorphs present ranged from 2–5 for each of these loci, and the frequency of each electromorph was averaged across all 13 samples. This is admittedly a simplification in that the averaged frequencies eliminate the impact of intersample variability in the ancestral population, but we take the position that small founder groups drawn from an ancestral large, relatively panmictic unit will offer the greatest chance of establishing a strongly underdominant rearrangement (Templeton, 1980). Additionally, the mean allele frequencies over all sampled subpopulations is generally regarded as a sufficient estimator of those for the ancestral population (Jacquard, 1974). We stress that this is simply our working model, and we wish to know the effects of extinction/recolonization on the likelihood of rearrangement fixation and its population genetic consequences, when beginning with a single large random-mating unit.

Natural history data on generation time, age at first maturity, and survivorship are not available for *S. grammicus*, but this species is a viviparous fall breeder (Guillette et al., 1980; Guillette and Casas-Andreu, 1980, 1981) and was therefore inferred to have life history traits similar to another viviparous fall-breeding species of *Sceloporus* for which such data are available. We used life table data available for high elevation (2545 m) populations of *S. jarrovi* from the Chiricahua Mountains in Arizona (Ballinger, 1973, 1979) to establish the maximum breeding age (4 yr) and an initial breeding age

TABLE 1. THE NUMBER OF EXTINCTIONS AND FIXATIONS FOR A SINGLE MUTANT CHROMOSOMAL REARRANGEMENT (B) AND THE ORIGINAL ARRANGEMENT (A) AFTER 100 BREEDING PERIODS IN 10 REPLICATES OF 20 POPULATIONS UNDERGOING REPEATED BOTTLENECKS. Bottleneck size was varied at 5, 10, and 20 individuals, and population size expanded to a maximum of 50, 50, and 100 individuals, respectively, before the population was re-bottlenecked to its original founder size. S represents the fecundity reduction in females heterozygous for the mutant rearrangement, and was set at 0.0, 0.025, 0.05, 0.10, and 0.25 for all simulations. Females had four offspring per breeding period if  $S = 0$ . n represents the total number of populations (of 200 possible) undergoing extinction or fixation of rearrangement A or B. Numbers in parentheses in these last two categories represent the number of populations surviving post-fixation extinction to the end of the simulation.

Initial founder size; fecundity reduction for chromosome heterozygotes	n (subsequent survivors)	Average no. of breeding periods (2 SE)	Average no. of bottlenecks (2 SE)	Population size (N) (2 SE)
I. 5 Founders:				
S = 0.00				
Extinct	162	43.1 (4.54)	10.3 (0.11)	3.5 (0.29)
Fix A	166 (34)	8.3 (1.42)	1.7 (0.36)	8.6 (1.25)
Fix B	16 (4)	24.1 (5.84)	5.4 (1.46)	7.5 (2.66)
S = 0.025				
Extinct	147	36.7 (4.64)	8.7 (1.12)	3.7 (0.30)
Fix A	157 (48)	8.8 (1.68)	1.8 (0.42)	8.2 (1.12)
Fix B	17 (5)	2.8 (6.84)	6.6 (1.66)	6.4 (1.60)
S = 0.05				
Extinct	156	40.5 (4.34)	9.6 (1.06)	3.4 (0.30)
Fix A	169 (40)	8.5 (1.64)	1.7 (0.41)	7.6 (0.88)
Fix B	10 (4)	31.4 (8.42)	7.3 (1.86)	7.6 (4.35)
S = 0.10				
Extinct	160	37.5 (4.61)	8.7 (1.12)	3.5 (0.32)
Fix A	167 (38)	7.1 (1.08)	1.3 (0.25)	8.3 (1.13)
Fix B	14 (2)	23.5 (5.23)	4.8 (1.32)	7.2 (2.53)
S = 0.25				
Extinct	155	37.1 (4.47)	8.8 (1.10)	3.3 (0.30)
Fix A	166 (39)	8.5 (1.34)	1.7 (0.33)	8.0 (0.96)
Fix B	9 (4)	23.3 (3.36)	5.2 (0.44)	5.2 (0.44)
II. 10 Founders:				
S = 0.00				
Extinct	22	51.3 (13.26)	16.8 (4.27)	6.6 (1.06)
Fix A	191 (169)	9.9 (1.81)	2.9 (0.60)	14.3 (1.28)
Fix B	7 (7)	43.9 (19.62)	13.4 (6.93)	12.7 (4.94)
S = 0.025				
Extinct	18	59.6 (16.30)	19.1 (5.29)	6.2 (0.94)
Fix A	188 (172)	8.5 (1.45)	2.3 (0.48)	14.7 (1.16)
Fix B	8 (8)	62.6 (15.82)	20.0 (5.26)	10.9 (1.75)
S = 0.05				
Extinct	16	47.4 (13.98)	14.9 (4.78)	6.3 (1.54)
Fix A	192 (178)	8.5 (1.52)	2.3 (0.48)	14.7 (1.23)
Fix B	6 (6)	31.7 (5.20)	9.7 (1.76)	21.7 (11.48)
S = 0.10				
Extinct	17	57.6 (15.28)	18.5 (5.05)	6.6 (1.21)
Fix A	193 (177)	8.1 (1.50)	2.1 (0.46)	14.4 (7.15)
Fix B	6 (6)	42.7 (12.84)	12.8 (3.70)	12.7 (5.33)
S = 0.25				
Extinct	25	44.6 (11.16)	14.4 (3.85)	6.5 (0.79)
Fix A	194 (171)	5.7 (0.64)	1.3 (0.20)	14.5 (1.18)
Fix B	4 (4)	34.5 (12.50)	9.7 (4.78)	25.0 (5.00)

TABLE 1. CONTINUED.

Initial founder size; fecundity reduction for chromosome heterozygotes	n (subsequent survivors)	Average no. of breeding periods (2 SE)	Average no. of bottlenecks (2 SE)	Population size (N) (2 SE)
III. 20 Founders:				
S = 0.00				
Fix A	192 (192)	11.3 (2.18)	3.4 (0.74)	29.5 (2.45)
Fix B	4 (4)	54.5 (7.00)	18.5 (1.00)	20.0 (0.00)
S = 0.025				
Fix A	196 (196)	9.9 (1.74)	2.9 (0.58)	29.3 (2.21)
S = 0.05				
Extinct	1	18.0 (—)	—	—
Fix A	196 (195)	7.6 (1.20)	2.0 (0.39)	30.9 (2.46)
S = 0.10				
Fix A	200 (200)	7.1 (1.00)	1.9 (0.33)	29.1 (2.34)
S = 0.25				
Fix A	200 (200)	5.3 (0.49)	1.2 (0.17)	30.9 (2.50)

(2 yr) for each individual in the population. The probabilities of survival from one breeding age to the next (in years) were: 0–1 = 0.2; 1–2 = 0.5; 2–3 = 0.7; 3–4 = 0.35; and >4 = 0.0 (Ballingier, 1973). The number of offspring for each female in each breeding period was set at four, on the basis of the number of near-term embryos taken from a total of 20 gravid *S. grammicus* collected in central Mexico during the summer of 1985. These lizards were collected from four medium-elevation localities (~2000 m) in the vicinity of Mexico City and Pachuca, Hidalgo (n = 13, litter sizes = 2, 3, 4, 4, 4, 4, 4, 4, 5, 6, 7, and 7) and two high-elevation sites (~3000–3900 m) east of Mexico City (n = 7, litter sizes = 3, 4, 4, 4, 4, and 5). Despite the altitudinal differences, all of these populations are from the same chromosomal race (the presumed ancestral 2n = 32; Hall, 1980, 1983; Porter and Sites, 1986) and are genetically very similar (Sites et al., 1988). The fecundity rate of four young per brood was fixed unless a female incurred a loss of fitness due to chromosomal heterozygosity.

The effect of structural chromosomal heterozygosity on fecundity in *S. grammicus* is poorly known. A few meiotic data are available for males heterozygous for simple Robertsonian rearrangements, and non-disjunctional frequencies range from 0.0–7.1% (Porter and Sites, 1985, 1987). Some data for fusion polymorphisms in mammals also generally show low levels of meiotic non-disjunction, although aneuploid frequencies of 25–30% are known for some rearrangements in *Mus* (de Boer, 1986).

Given this range of values for vertebrates, we carried out all simulations for fecundity reduction levels of 0.0, 0.025, 0.05, 0.10, and 0.25 for females heterozygous for single rearrangements. These values seem likely to encompass those possible in natural populations of *S. grammicus*. Simulations were conducted for minimum-maximum population sizes of 5–50, 10–50, and 20–100 individuals. The model assumes that: 1) survivorship is only a function of age (above-given life table probabilities) and that all individuals have an equal opportunity to produce offspring; 2) fitnesses are equal between the ancestral and derived chromosomal homozygotes; 3) sampling was random with respect to sex; and 4) the breeding units are completely isolated from each other, a condition that enhances fixation times and probabilities (Lande, 1979; Slatkin, 1981) and speciation (Walsh, 1982).

## RESULTS

The results of our simulations are summarized in Tables 1 and 2. All three population genetic parameters in Table 2 were regressed on the independent variables of mean number of bottlenecks, and mean number of breeding periods for each simulation. The coefficients of determination ( $R^2$ ) for regressions of genetic parameters on average time (in breeding periods) since last bottleneck, and average number of breeding periods between bottlenecks, showed that very little of the total variation was explained by either of these relationships.

TABLE 2. MEAN VALUES FOR NEI'S (1972) GENETIC DISTANCE (D) AND WRIGHT'S (1965)  $F_{IS}$  AND  $F_{ST}$  STATISTICS RELATIVE TO MEAN NUMBER OF BOTTLENECKS IN EACH SIMULATION.

Initial founder size: selection against chromo- somal heterozygotes	D	$F_{IS}$	$F_{ST}$
I. 5 Founders:			
S = 0.00	0.308	0.491	0.488
S = 0.025	0.265	0.484	0.519
S = 0.05	0.228	0.369	0.511
S = 0.10	0.283	0.347	0.554
S = 0.25	0.245	0.402	0.513
II. 10 Founders:			
S = 0.00	0.151	0.055	0.680
S = 0.025	0.144	0.097	0.639
S = 0.05	0.153	0.022	0.672
S = 0.10	0.152	0.002	0.677
S = 0.25	0.149	0.038	0.673
III. 20 Founders:			
S = 0.00	0.102	-0.039	0.493
S = 0.025	0.110	-0.037	0.516
S = 0.05	0.112	-0.036	0.509
S = 0.10	0.111	-0.038	0.511
S = 0.25	0.118	-0.037	0.510

(Complete regression statistics are available from JWS, Jr. upon request.)

When the number of founders is five, extinction is the fate of most populations (73–81%), regardless of fecundity reductions imposed by chromosomal heterozygotes (Table 1). Column five in Table 1 indicates extinctions usually occurred when founder populations had been reduced to less than four individuals ( $n = 3.3$ – $3.7$ ) and likely were fixed for one sex. These populations initially persisted for over 35 generations and survived at least eight bottlenecks before going extinct (columns 3 and 4). Not surprisingly, the majority of surviving demes became fixed for the original chromosomal arrangement (A), and this occurred after an average of 7–8 breeding periods and less than two bottlenecks. Population sizes were generally around eight individuals. A few demes fixed the new rearrangement (B), and these comprised anywhere from 1% (for  $S = 0.10$ ) to 2.5% (for  $S = 0.025$ ) of the total number of populations. This proportion of populations fixing and surviving with the novel arrangement indicates that size of the founder population was the factor of overriding importance relative to fecundity reduction values. This outcome showed the larg-

est variance in average number of breeding periods before fixation (2.8–31.4), and generally occurred after 5–7 bottlenecks. Interestingly, population sizes at which fixation of alternate chromosomal rearrangements occurred were significantly different, as inferred by nonoverlap of standard error terms, only when  $S = 0.25$  ( $n = 8.0 \pm 0.96$  for A,  $5.2 \pm 0.44$  for B). This type of population structure also had the most distinctive overall electrophoretic "signature," with D values ranging from 0.228–0.309,  $F_{IS}$  from 0.347–0.491, and  $F_{ST}$  from 0.488–0.554 (Table 2). The regression of D on mean number of bottlenecks explains successively smaller fractions of the total variation from neutral ( $R^2 = 0.471$ ) to the most underdominant rearrangement ( $R^2 = 0.34$  for  $S = 0.25$ ).  $F_{IS}$  and  $F_{ST}$  values showed generally the same trends when regressed on both mean number of bottlenecks and number of breeding periods between bottlenecks.

When the number of founders is increased to 10 individuals while the same maximum population size is retained ( $n = 50$ ), the proportion of demes going extinct predictably declines (8–12%). Overall trends for populations fixing the original chromosomal arrangement and surviving 100 breeding periods can be summarized as follows relative to simulations of smaller founding populations. The average number of breeding periods (5.7–9.9) and average number of bottlenecks (1.3–2.9) approximate those values for simulations with five founders. The population size ( $=n$ , or census size) at fixation is 14–15 individuals, and the proportion of demes surviving 100 generations ranges from 0.88–0.93%. Populations fixing the alternate arrangement all survive extinction, and comprise anywhere from 2% ( $S = 0.25$ ) to 5% ( $S = 0.025$ ) of the total number of populations. Notice, however, that the vast majority of populations survive with the original chromosomal configuration. The average number of breeding periods (31.7–62.6) and number of bottlenecks (9.7–20.0) prior to fixation are both larger than in simulations for five founders, but usually have large error terms. The  $n$  at which fixations occur vary from 10.9–25.0, are associated with large error terms, and, surprisingly, fixation for the most underdominant rearrangement occurs at a relatively large population size ( $n = 25$  for  $S = 0.25$ ). This is likely the result of sampling error increasing the frequency of the new rearrangement above 50%, and then selection driving it to fixation. Such an event is independent of the strength

of underdominance for the rearrangement. The genetic distances and inbreeding coefficients decrease, but so does the range (and by inference, the variance) of  $D$ ; values range from 0.144 ( $S = 0.025$ ) to 0.153 ( $S = 0.05$ ).  $F_{IS}$  ranges from 0.002 ( $S = 0.10$ ) to 0.097 ( $S = 0.05$ ), while  $F_{ST}$  values unexpectedly increase, ranging from 0.63 ( $S = 0.025$ ) to 0.680 ( $S = 0.00$ ). Regressions on both independent variables explained much more variation in  $F_{ST}$  and  $D$  values than in  $F_{IS}$  values.

Simulations for founder populations of 20 individuals expanding to a maximum population size of 100 showed negligible extinction events and no fixations for the alternate rearrangement at four of the five values of  $S$ . For strictly neutral rearrangements ( $S = 0.00$ ), four of 196 populations (2%) fixed the novel mutation after an average of over 18 bottlenecks during 54+ breeding periods at  $n = 20$ .  $D$  values decrease to a range from 0.102 ( $S = 0.00$ ) to 0.118 ( $S = 0.25$ ), while  $F_{ST}$  values again show pronounced subdivision, ranging from 0.493 ( $S = 0.00$ ) to 0.516 ( $S = 0.025$ ).  $F_{IS}$  values are all slightly negative and differ only at the third decimal place for all values of  $S$  ( $-0.039$ – $-0.036$ ). Almost none of the variation in  $F_{IS}$  is explained by regression on the independent variables, while both account for 91–93% and 61–87% of the variation in  $F_{ST}$  and  $D$ , respectively.

#### DISCUSSION

Hall's cascading or chain speciation model for features correlated with rapid speciation in *Sceloporus* postulates that: "(1) Chromosomally differentiated species originate as very small founder populations. (2) The probability that chromosomal differentiation will occur at all is profoundly affected by: a) rates of chromosomal mutation, b) behavior of the chromosomes in meiosis and the genetic consequences of any meiotic errors, c) details of the species' mating system, and d) details of its population structure. (3) The aspects of a species' genetic system listed above are genetically controlled." (Hall, 1983). If loci determining these "genetic system parameters" are polymorphic, then some demes small enough to fix chromosomal rearrangements may also vary considerably in allele frequencies at these other loci, primarily due to drift. Thus, some demes will by chance have a more favorable background than others for fixing new rearrangements. Founder populations that survive and fix such a rearrangement will

tend to perpetuate this favorable genetic background, and be more likely to foster the continued establishment of additional rearrangements. Such a scenario appears to strongly parallel Slatkin's (1977) propagule-pool model of founding new populations, in which new founder individuals are all drawn from the same ancestral population. Given adequate levels of heterozygosity in the ancestral population (Templeton et al., 1981), these types of founder events are expected to produce appreciable between-deme genetic differentiation (Maruyama and Kimura, 1980). Hall (1983) also comments "The founder population required for the chance fixation of a negatively heterotic chromosomal rearrangement is ideal for other stochastic phenomena such as the random fixation or drift of alleles at a variety of polymorphic gene loci."

Given the repeated extinction-colonization cycles required to fix and spread underdominant rearrangements (Lande, 1979, 1985), our simulations suggest that founding populations of five individuals seem to offer the greatest possibility for promoting speciation by the cascade mechanism. Extinction rates were very high, and only a small proportion of all demes survived to fix a new rearrangement (1–2.5%, Table 1). Demes fixing rearrangement B, however, represented 5.2–11.7% of all surviving demes. Note that these values are very close to the expected probability for fixation of a neutral mutation in a diploid organism with a beginning founder size of  $n = 5$  (probability =  $1/10$ ), regardless of the actual strength of selection against the heterozygote. Thus at very small founder size, a strongly underdominant rearrangement—the only kind that could be effective at promoting chromosomal speciation by either the stasipatric (White, 1978) or cascade (Hall, 1983) mechanism—is just as likely to be fixed and avoid extinction as is a strictly neutral rearrangement, and that this level of fixation (~5–10%) would be high enough to be important over evolutionary time (i.e., thousands of breeding periods vs 100). The average number of breeding periods to fixation of rearrangement B was less than 25 in all but one case (where  $S = 0.05$ , Table 1), suggesting that the retention time for the AB polymorphism in a subpopulation would be very brief. This type of population structure leaves a very distinct profile with respect to interdeme genetic distances ( $D$ ), degree of subdivision ( $F_{ST}$ ), and inbreeding ( $F_{IS}$ ), which differs markedly from those

actually obtained for 13 natural populations of *S. grammicus*. The D values in the pairwise matrix (Sites and Greenbaum, 1983) ranged from 0.003–0.112 ( $\bar{x} = 0.031$ ),  $F_{IS}$  values ranged from  $-0.381$ – $0.195$  ( $\bar{x} = -0.007$ ), and  $F_{ST}$  ranged from 0.015–0.755 ( $\bar{x} = 0.135$ ) (Thompson and Sites, 1986). The D values presented in Sites and Greenbaum (1983) were calculated from a total of 19 loci and with a slightly different algorithm. When only the 15 loci used in these simulations are used to calculate the Nei (1972) D coefficient, values are altered slightly, but only in the third decimal place. These D values range from 0–0.095 ( $\bar{x} = 0.026$ ); (a complete matrix of these values is available from JWS, Jr. upon request). The natural populations appear to be considerably less structured than those of simulated demes, and the high positive  $F_{IS}$  values in the latter suggest that the small size of the bottlenecks fostered high inbreeding. This may be facilitated by overlapping generations and the possibility of matings between age classes (Giesel, 1971).

When the bottleneck size is 10 individuals, the number of demes surviving with the new rearrangement represents 2.3–4.6% of all surviving demes. This is due to lower extinction rates and a much higher survivorship of breeding groups fixing the original rearrangement, but again these probabilities are close to strictly neutral expectations for a diploid organism with 10 founders ( $=\frac{1}{20} = 5\%$ ). The genetic profile is considerably different from that for the 5-founder scenario in that  $F_{IS}$  values generally decrease by nearly an order of magnitude, suggesting little or no inbreeding, and D values decrease by approximately half (Table 2). D values are still much higher than the empirical results, and  $F_{ST}$  increase considerably. The larger  $F_{ST}$  values suggest that a larger founding population size perhaps permits many alternate low-frequency alleles to remain in some populations long enough to be fixed, while being lost from other breeding groups. This would be especially important in 3–4 allele loci and could have a strong impact on  $F_{ST}$ . The founders of  $n = 5$  likely result in rapid loss of almost all rare alleles early on in a series of extinction-recolonization events.

For both of these sets of simulations the size of the root-mean-squared error terms for D,  $F_{IS}$ , and  $F_{ST}$  values indicates considerable overlap among each of these correlates across all values of S. This implies that the degree of selection against the chromosomal heterozygote has vir-

tually no influence on fixation probabilities under these conditions, and that electrophoretic profiles will be virtually identical for populations fixing neutral versus strongly underdominant ( $S = 0.25$ ) rearrangements. These results are consistent with other simulations showing drift to be of overriding importance in small populations (Lacy, 1987).

With founder sizes of 20 animals, D values decrease to a range of 0.102–0.118, which overlap to some extent with the empirical results. The D values increase slightly with increasing selection against the chromosomal rearrangement, as predicted for some chromosomal speciation modes (Templeton, 1980), but there is enough overlap in the error terms ( $D = 0.102 \pm 0.017$  for  $S = 0$ ;  $D = 0.118 \pm 0.030$  for  $S = 0.25$ ) to obscure any distinction in electrophoretic profile between these extremes. From a statistical standpoint, the estimates are all the same, as judged from overlap in error terms. Under constraints of our model, the genetic structure of the *S. grammicus* populations sampled by Sites and Greenbaum (1983) most nearly approximates the simulations having the largest bottleneck and maximum population sizes (20, 100) for D and  $F_{IS}$ , but in such a population, only neutral or nearly neutral rearrangements have any appreciable probability of fixation (Table 1).

If our simulations are realistic, we must conclude that the cascading model of chromosomal speciation is unlikely for *S. grammicus* in its present form; the empirical and simulated electrophoretic profiles are far too different. This conclusion corroborates the empirically-based population genetic (Sites and Greenbaum, 1983; Thompson and Sites, 1986) and cytogenetic studies (Sites, 1983; Porter and Sites, 1986, 1987), but is of course subject to caveats of the model. To simplify the model, we effectively homogenized the ancestral population by taking all alleles present at each polymorphic locus summarized by Sites and Greenbaum (1983), and averaging their frequencies across all samples. This of course eliminates the impact of ancestral interlocus variability on calculations of subsequent genetic measures, but such an impact would also have to be considered in light of other interactive factors such as gene flow, mutation rate, and the possible influence of disruptive selection, positive heterosis, or directional selection for the novel chromosomal homozygote. The behavior of D, for example, is a function of the number of allelic states per

locus, which has been maximized by our averaging assumption, levels of between-deme gene exchange (held to zero here), and equality/inequality of between-deme mutation rates (not considered). While it is beyond this discussion to explore all possible combinations of these factors, we can offer a few generalizations. At some level, often very low (Futuyma and Mayer, 1980; Lacy, 1987), gene flow between breeding units would reduce levels of divergence ( $D$ ) and inbreeding ( $F_{IS}$ ), but also decrease the probability of fixing all but neutral or positively heterotic rearrangements (Lande, 1979, 1984). Our model maximizes the probability of fixing strongly underdominant rearrangements (Walsh, 1982; Lande, 1985), but is probably unrealistic in its assumption of no interpopulation gene exchange. Gene exchange would also be expected to lower  $F_{ST}$  values, although significant between-population allele-frequency heterogeneity can be maintained in the face of appreciable gene flow (Allendorf and Phelps, 1981).

We have also ignored mutation rates, and it has been shown in other organisms that such can be considerably influenced by hybrid dysgenic events and transposable element activity (Bregliano and Kidwell, 1983; Collins and Rubin, 1984), and that disruptive effects of hybridization may often be manifested as increased rates of chromosomal rearrangement (Shaw et al., 1983; Hagele, 1984; Naveira and Fontdevila, 1985). Given the known and potential areas of hybridization between cytotypes in the *S. grammicus* complex (Sites and Davis, unpubl.), it is conceivable that strong geographic variation in mutation rates could develop, and perhaps have a pronounced influence on the rates of fixation of new rearrangements in some populations.

These simulations are admittedly limited in scope and parameters examined, and they represent a first attempt to explore some genetic consequences of some evolutionary forces acting to fix new chromosomal rearrangements. The results generated can at best serve only as an approximate null model for interpreting potential natural examples of chromosomal speciation and their associated population structures and genetic correlates. The *S. grammicus* complex may be one example of some type of chromosomal speciation, but the possible mechanisms and explanations are extensive (Sites and Moritz, 1987), and considerable empirical and theoretical work remains to be done.

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