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Evolutionary Significance of Genetic Diversity in Nature: Environmental Stress, Pattern and Theory

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21.1 The Ecological-Genetics Theater and the Evolutionary Play

21.1.1 Ecological-genetics Interaction and Evolution

The dynamics of the twin evolutionary processes of adaptation and speciation is dependent on the ever-changing ecological theater and its interaction with the participating organism players. This environmental-organism ongoing drama is based on the underlying molecular structure and differentiation of genetic diversity at the DNA level and its derivative proteins which drive the biochemical machinery of the organism. Therefore, genetic diversity within and among species is central to evolutionary biology, i.e., to the origin of adaptations and species in nature [Nevo 1988a]. Molecular biology permitted the characterization of genetic diversity among individuals, populations and species [Lewontin 1974]. Thus, the road was opened to relate genotypes and phenotypes, and highlight the continuum from micro- to macro-evolution. The elucidation of genetic diversity and its dynamics in nature permitted the remarkable developments in ecological and modern evolutionary genetics and broadened our understanding of the evolutionary process.

21.1.2 Genetic Diversity in Nature: An Overview

Genetic diversity in nature became known mainly in population genetics by isozyme diversity studies in plants, animals and humans [Lewontin 1974] and was only later followed by DNA diversity analyses [Nevo 1988a]. Spectacular developments occurred since the recognition of the biological significance of isozymes - i.e., multiple molecular forms of enzymes [Markert and Moller, 1959]. Hundreds of theoretical and applied isozyme studies were conducted since the origin of the isozyme concept. Many of the theoretical studies were reviewed and reanalyzed by Nevo [1978] and others, and later a comprehensive overview was conducted by Nevo et al, [1984a], and Nevo [1988a,b].

21.1.3 Protein and DNA Studies at the Institute of Evolution

Many papers and reviews were published describing local and regional studies conducted during 15 years [1977-1992] at the Institute of Evolution, University of Haifa [Nevo 1983a, 1986a, 1988b, 1989a, 1990, 1991, 1992a], including a global data set [Nevo et al, 1984a]. Here I will overview the local, regional and several global isozyme analyses conducted at the Institute of Evolution through 1992. This review will (i) include micro- and macro-geographical protein and DNA studies conducted during 1989-1992; and (ii) reaxamine and generalize some of the earlier data sets in terms of several novel evolutionary perspectives, primarily environmental range and stress. My main concern in the present review is to answer the major evolutionary question: "what degree of isozyme polymorphism, or more generally, genetic diversity in nature, is the basis of adaptive evolutionary change"? [Lewontin 1974]. I will show that in contrast to the claim of the neutral theory of molecular evolution [Kimura, 1983], a substantial proportion of isozyme polymorphism in nature is adaptive and being maintained and oriented primarily by natural selection.

The nature of isozyme diversity, or protein and DNA diversities in general, is still under heated debate [see Nevo, 1990 and references therein]. One major reason for the ongoing debate of whether molecular polymorphisms are primarily neutral, nearly neutral or mainly adaptive, is the scarcity of ecology in population genetics studies. Clearly, if the basic parameters of evolutionary dynamics in nature are unknown (mutation, recombination and migration rates over space and time) the easy solution is to ignore current evidence and assume the unknown parameters. The better alternative, of course, is to ask how much of allozyme diversity in nature is explained by physical and biotic factors. Our studies in natural populations of plants and animals have been aimed at unravelling the ecological factors explaining genetic diversity in nature.

We analyzed diverse ecological spectra at local, regional and global geographical scales. Furthermore, we used both post-hoc and pre-hoc controlled laboratory experiments [Nevo, 1986b, 1990]. Here I will briefly overview studies attempting to draw generalities across phylogeny and ecological spectra in terms of molecular evolutionary genetics. Our main research strategy was to employ diverse environmental-physiological stresses which substantially affect genetic diversity and differentiation.

21.2 The Environmental Range and Stress Strategies

Environmental range and stress dramatically affect molecular diversity and its differentiation at both the protein and DNA levels leading to evolutionary change [Parsons, 1991 and references therein]. We investigated in our micro- and macro-geographical studies the niche-width variation hypothesis [Van Valen, 1965] utilizing evidence derived from the following abiotic and biotic stresses: (i) aridity; (ii) thermal; (iii) salinity; (iv) chemical; and (v) biotic.

21.2.1 Aridity Stress on Isozyme and DNA Diversity at Local, Regional and Global Geographic Scales

Drought stress affects all life aspects [Evenari et al, 1985, 1986]. Indirect evidence for climatic selection in nature, at both the molecular and organismal levels, was reviewed in Nevo [1992a]. Two complementary approaches have been utilized, in studies conducted at the Institute of Evolution. First, the demonstration of genetic parallelism in unrelated species sharing similar ecologies [Nevo and Beiles, 1988]. Second, the demonstration of genotypic and phenotypic differentiation in closely related species distributed over different ecologies [Nevo, 1991]. The correlations of heterozygosity with aridity stress and climatic unpredictability in the first case, and the clinal geographic variations at all organizational levels in the second case, suggest natural selection as a principal causal factor. Climatic selection, or more specifically, aridity stress, appears to be a major direct and/or indirect cause of selection in natural populations. Israel can be viewed as an ecological theatre where, over very short distances, the rapid change in aridity stress plays a major evolutionary role in genetic and phenotypic differentiation of populations and species [Nevo, 1986a]. Our studies concerning the effects of aridity stress on the level, pattern and differentiation of genetic diversity (isozymes, nuclear and mitochondrial DNA) was reviewed by Nevo [1978, 1983a, 1988b, 1989a,b, 1992a]. These studies included both plants and animals, and were conducted on both micro- and macro-geographical scales that will now be briefly overviewed.

21.2.1.1 Micro-geographical isozyme studies

In the microsites studies across Israel, we analyzed protein (primarily isozyme) diversity in wild cereals including wild oats [Kahler et al, 1980], wild barley [Nevo et al, 1981a, 1983a, 1986a,b], wild emmer wheat [Nevo et al, 1988a,b, 1991a] and landsnails [Nevo et al, 1981b, 1982]. These microsite studies involved the effect on allozymes among different rock, soil and slope types and microclimates (for examples, we compared landsnailes on opposing wadi slopes varying in the amount of radiation and hence in heat and drought; For wild emmer wheat see Figs. 1 and 2 as an example of the Ammiad microsite study [Nevo et al, 1991a] and Figs. 3 and 4 representing the Tabigha microsite study). Our tests involved both single loci as well as two-locus gametic phase disequilibria (Fig. 4), multilocus structures [Brown et al, 1980; Golenberg and Nevo, 1987] and genome organization. Some tests were repetitive, involving short transects (100 meters; e.g., [Nevo et al, 1988b]; and Fig. 3); mosaic configurations simulating an ecological archipelago [Nevo et al, 1991a] (Fig. 1); and distinctly different opposing wadi slopes [Nevo et al, 1982].

21.2.1.2 Macro-geographical Regional Isozyme Studies

Studies of regional aridity stress were conducted across Israel as a "biological laboratory" [Nevo, 1986a]. The entire country represents an aridity stress and climatic unpredictability theater where both factors increase primarily southward towards the Negev desert (Figs. 5-7), and secondarily, eastwards towards the Rift Valley [Nevo, 1983a; Nevo and Beiles, 1988]. Climatically, Israel is subdivided by one of the world's major climatic borders which divides the country into two distinct integrading parts: the northern mesic Mediterranean area and the southern xeric steppes and deserts. The coefficient of variation of rainfall increases southwards reinforcing the aridity stress, and creating the worst of all possible worlds: climatic stress and unpredictability. Consequently, phyto-geographically, Israel involves three major regions: the mesic Mediterranean, steppic Irano-Turanian, and desert Saharo-Arabian regions [Atlas of Israel 1970: climatic, geological, edaphic and vegetational maps]. This climatic and wide ecological diversity support a remarkably rich biotic and genetic diversity. Our regional aridity studies included wild oats [Kahler et al, 1980], wild emmer wheat [Nevo and Beiles, 1989], wild barley [Nevo et al, 1986a; Nevo, 1992b] and 21 species across Israel [Nevo, 1983a; Nevo and Beiles, 1988].

***Figure 1:** Genetic diversity, He, based on 43 loci in 11 vegetationally and topographically defined subhabitats of wild emmer wheat, Triticum dicoccoides, at the Ammiad microsite in northern Israel [from Nevo et al, 1991a].*

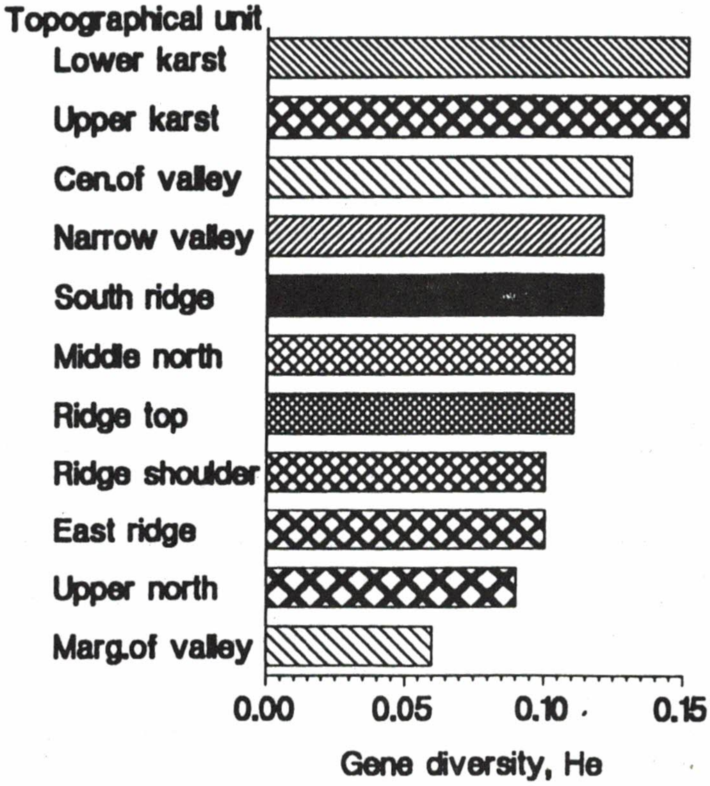
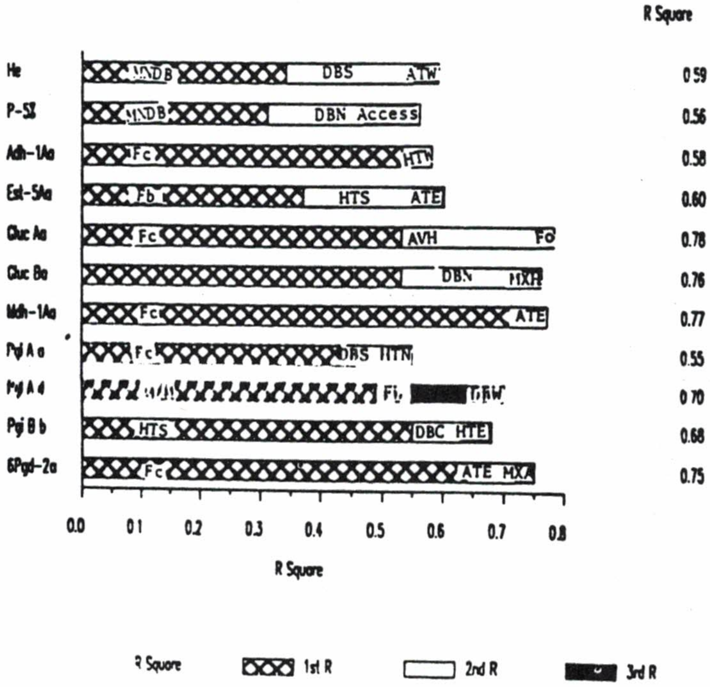


***Figure 2:** Coefficients of multiple regressions (R2) of genetic diversity (He, P and selected allelic frequencies, as the dependent variables) and 22 micro-ecological variables (as independent variables) in 11 vegetationally and topographically defined subhabitats of T. dicoccoides, in three consecutive growing seasons at Ammiad [from Nevo et al, 1991a].*



Level of significance for all values = 0.001

Figure 3: Allele distribution of selected allozyme loci of T. dicoccoides along the 100m, two-soil-type transects at Tabigha, Israel. Ipol a; Pgi-A b; Pgm-A c [from Nevo et al, 1988b].

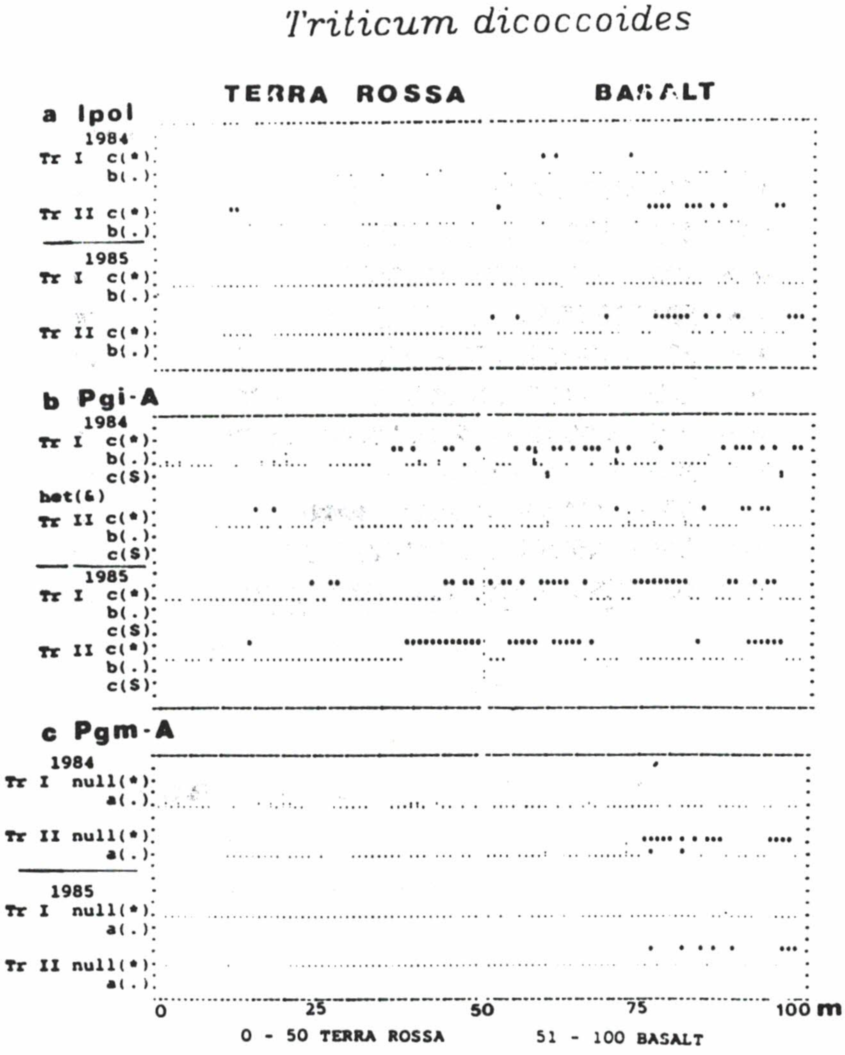


Figure 4: Gametic phase disequilibrium, D, between Mdh-1Aa and Acph-xa in 2 years and 2 transects of wild emmer wheat, Triticum dicoccoides, growing on two soil types at the Tabigha microsite [from Nevo et al, 1988b].

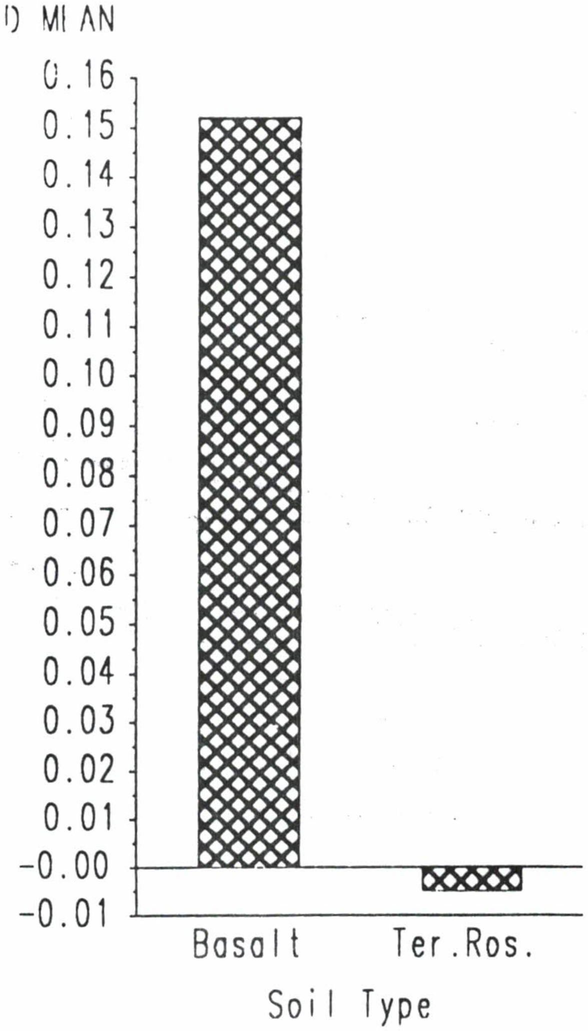


Figure 5: Parallel genetic patterns in the level of gene diversity, He, of unrelated genera represented by plants, invertebrates and vertebrates in Israel, plotted against increasing climatic unpredictability eastward and southward; represented by mean relative interannual variability of rainfall amount, expressed as fraction (RV) [from Nevo and Beiles 1988].

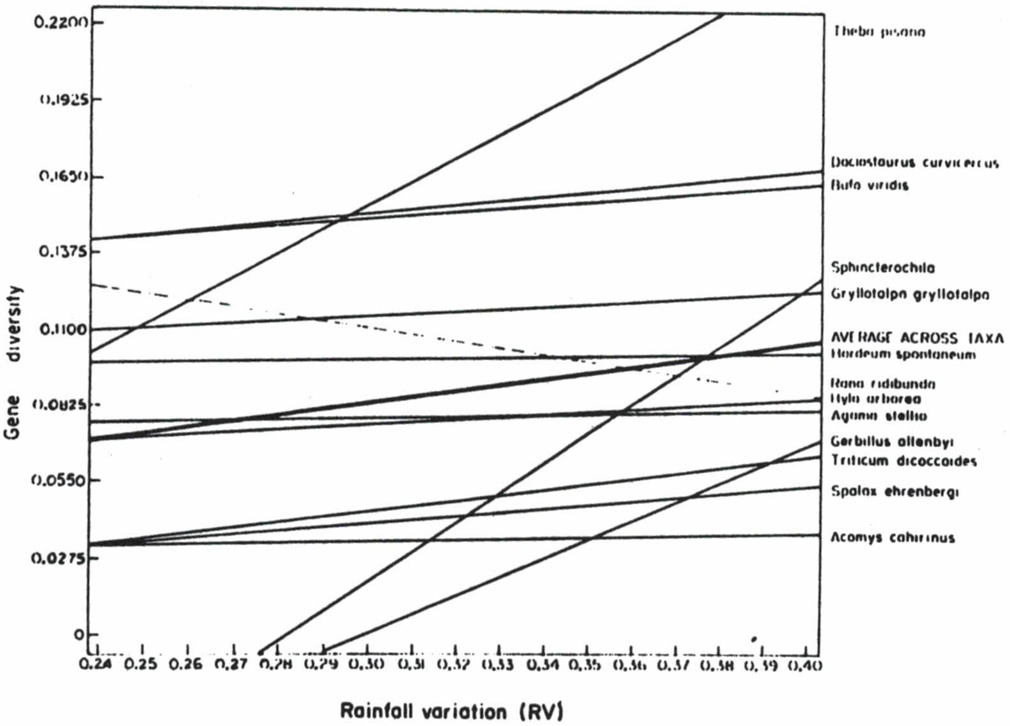


Figure 6: Parallel genetic patterns in the level of gene diversity, He, of 13 enzymatic systems averaged across all taxa studied here. A list of b-values (the slope) is displayed to the right of the enzyme names. The average line is: He = -0.0556 + 0.4803 RV [from Nevo and Beiles, 1988].

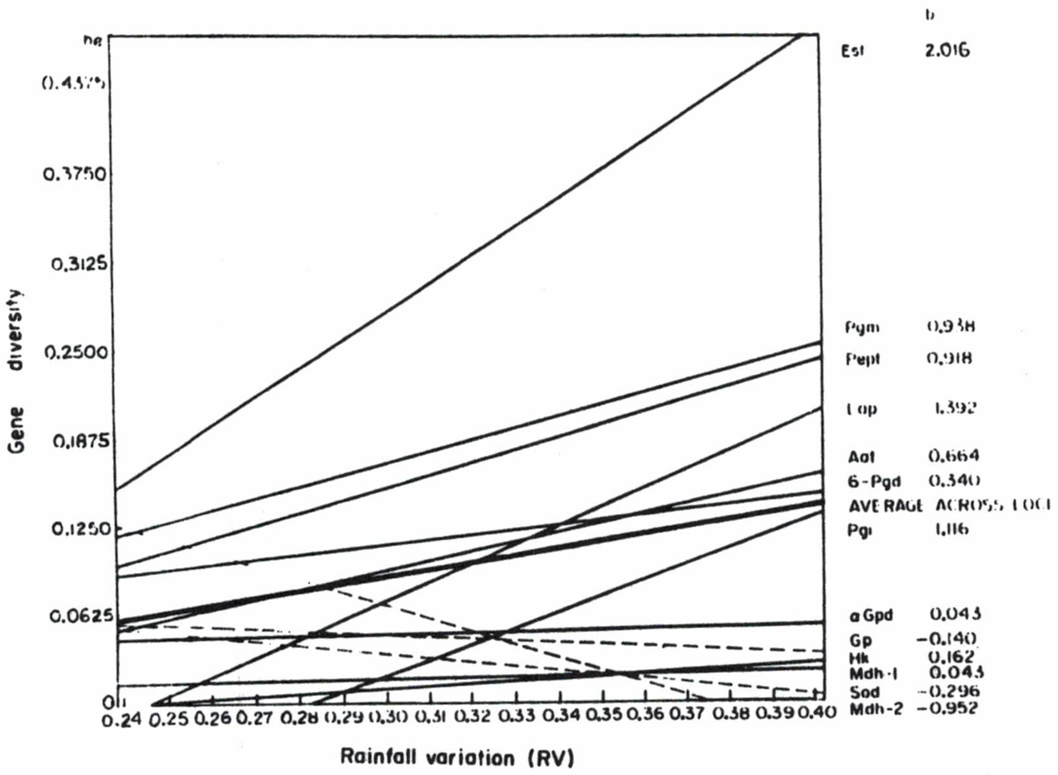
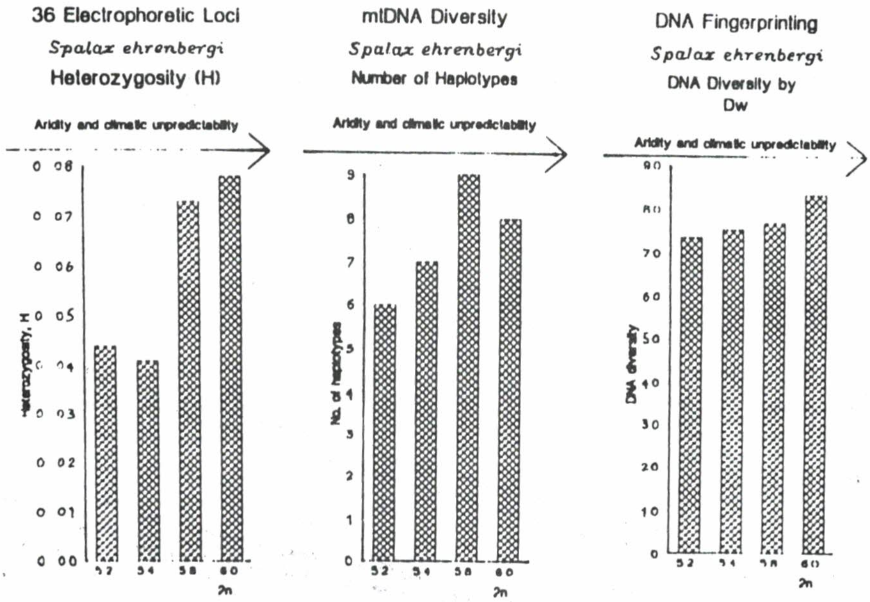


Figure 7: Comparisons of parallel genetic diversities in allozyme, mitochondrial DNA and DNA fingerprinting of the 4 chromosomal species of the Spalax ehrenbergi superspecies in Israel across an aridity gradient of 200 km southward towards the Negev desert [in preparation].



21.2.1.3 DNA Diversity Regional Studies

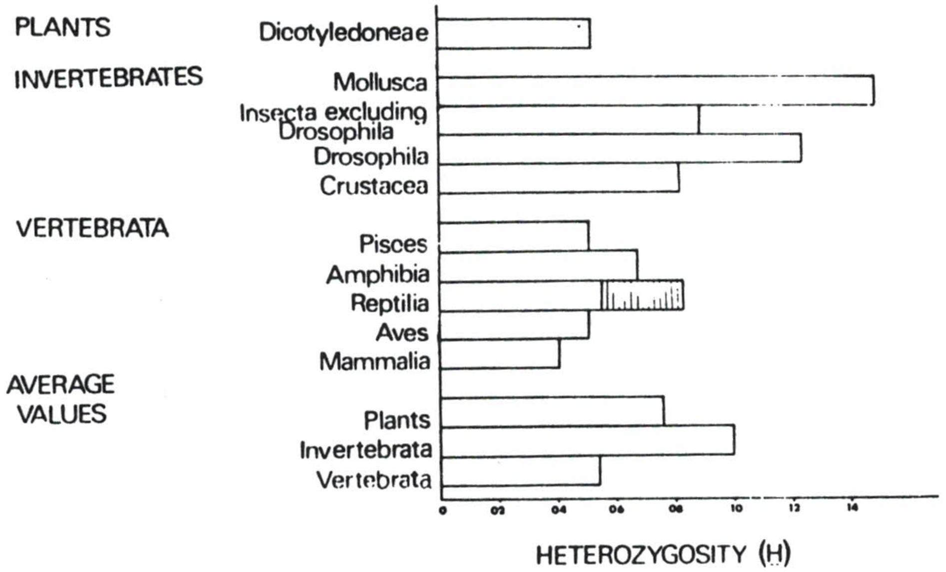
We have analyzed nine systems of nuclear and mitochondrial DNA diversities in the blind subterranean mole rats of the Spalax ehrenbergi superspecies in Israel [Nevo, 1991; and in preparation]. These studies involve the following systems: (1) the Major histocompatibility complex (Mhc); (2) ribosomal DNA nontranscribed- spacer polymorphism, rDNA NTS; (3) haptoglobins; (4) myosin heavy chain; (5) aldolases; (6) Per homologous sequence; (7) homeobox; (8) DNA fingerprints; (9) mitochondrial DNA; and (10) rDNA in wild emmer wheat [Flavell et al, 1986]. In all of these DNA diversity studies we found environmental correlates either with the physical (climatic, primarily aridity) or biotic (pathogens and parasites), diversities.

21.2.1.4 Macro-geographical global isozyme studies

Studies of global ecological, demographic and life historical patterns of genetic diversity including climatic diversity and aridity, were conducted first on 1111 species of plants and animals across the planet with climatic data for 425 species (Figs. 8-11). These live in arid, sub-arid, sub-humid, mesic, extra-mesic and mesic plus arid climatic regions [Table 8a in Nevo et al, 1984a].

Our second global study involved 184 small mammalian species, both insectivores and rodents, subdivided into above ground, fossorial and subterranean species [Nevo et al, 1990] (Fig. 12). Clearly, the species living above ground are living under higher aridity stress and climatic unpredictability than those living underground [Nevo, 1979]. The third global study involved 189 amphibian species (2 orders and 13 families), which included 123 urodeles (5 families) and 66 anurans (8 families) [Nevo and Beiles, 1991] (Figs. 13-14). These species

Figure 8: Global levels of genetic diversity among higher taxa [from Nevo et al, 1984a].



which occupy arid, subhumid, mesic and mesic plus xeric climatic regimes, include terrestrial, arboreal, aquatic and subterranean habitats.

The allozyme studies at the local, regional and global levels involved genetic indices of heterozygosity (H) and polymorphism (P) of populations and species averaging 25 loci (range, 10-50) analyzed per individual (Figs. 8-11). The following general results were obtained across all micro- and macro-geographic studies involving aridity stress.

Genetic diversity, both at the protein (mainly isozymes) and in several studies at DNA levels (both nuclear and mitochondrial DNA diversities) was nonrandom and massively structured, at single, multilocus and genome organization levels (Figs. 1-14); (ii) positively correlated with increasing aridity stress and climatic unpredictability (Figs. 5-7); (iii) species living in a broader climatic spectrum - i.e., in both mesic and arid environments-showed significantly higher level of heterozygosity (Figs. 1,5,6,7,10,12,14). This pattern, as the previous one, supports the niche width variation hypothesis [Van Valen, 1965] at the genetic level [Nevo, 1988b]; (iv) The global studies demonstrated that genetic diversity varies also with other ecological factors beside aridity stress (life zone, geographic range, habitat type and range); demographic parameters (species size and population structure, gene flow and sociality); and with a series of life history characteristics (longevity, generation length, fecundity, origin, and parameters related to the mating system and mode of reproduction) (Figs. 10 and 3a-c; 4a-c; 5a-c in Nevo et al, 1984a).

Generally, genetic diversity is higher in: (i) species living in broader environmental spectra, (ii) large species with patchy population structure and limited migration, as well as in social species, and (iii) species with the following characteristics: small body size, annuals or long-lived perennials, older in time, with smaller diploid chromosome numbers, primarily outcrossing; and plant species reproducing sexually and pollinated by wind. Species with the above characteristics harbor generally more genetic diversity than their opposite counterparts.

Genetic diversity in our largest global study [Nevo et al, 1984a] is partly correlated with

Figure 9: Frequency distribution of heterozygosity among higher taxa on a global scale [from Nevo et al, 1984a].

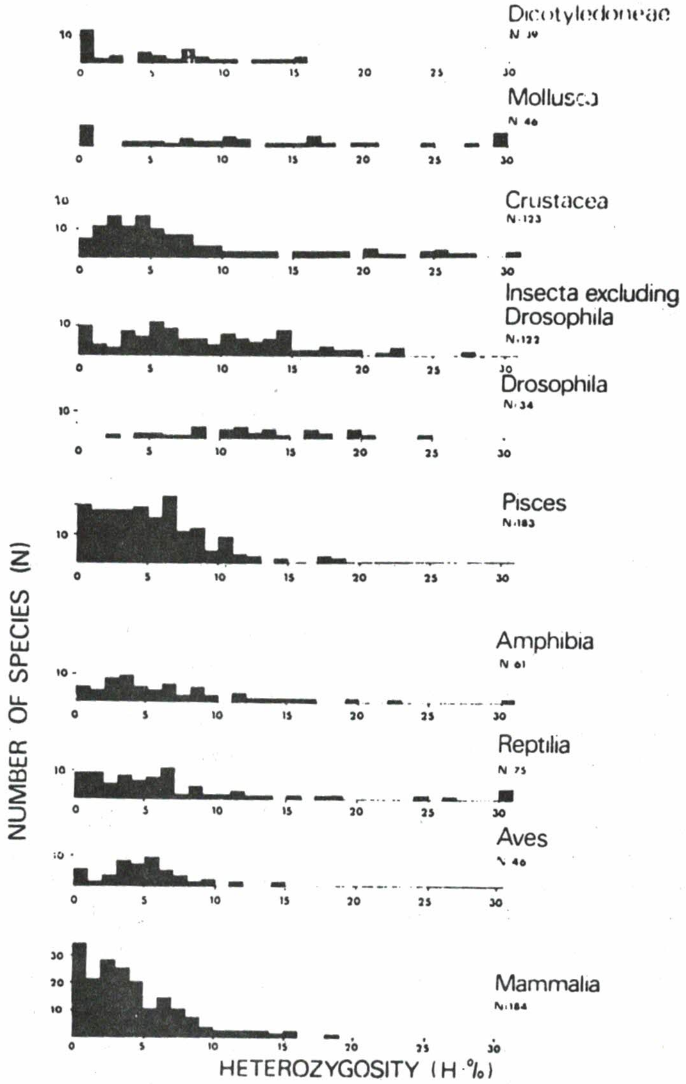


Figure 10: Global levels of heterozygosity of biotic ecological factors [from Nevo et al, 1984a].

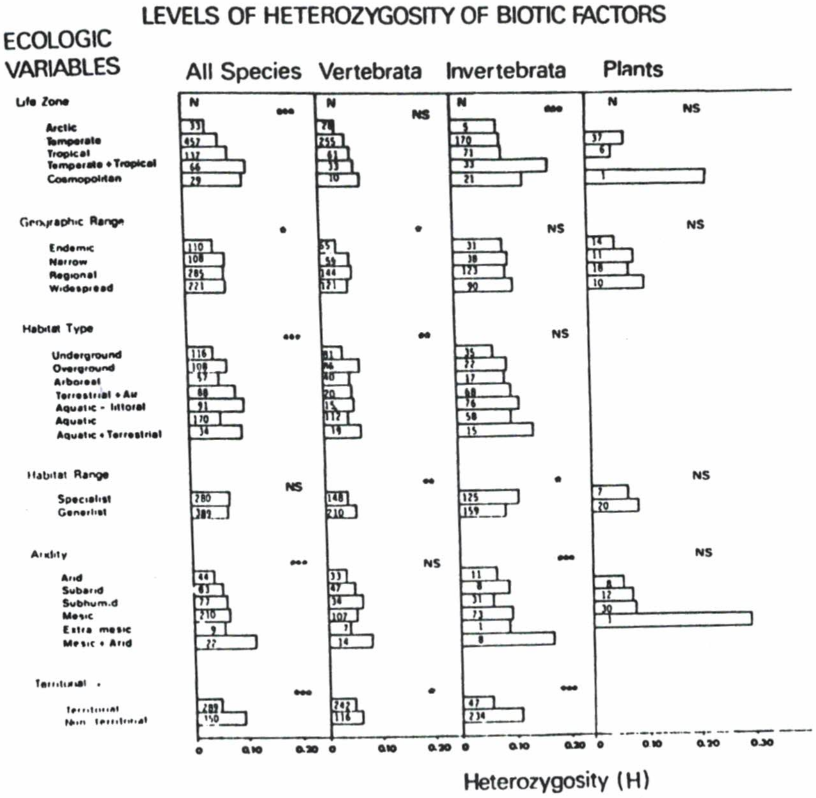


Figure 11: Explained portion of genetic diversity by biotic variables on a global scale [from Nevo et al, 1984a].

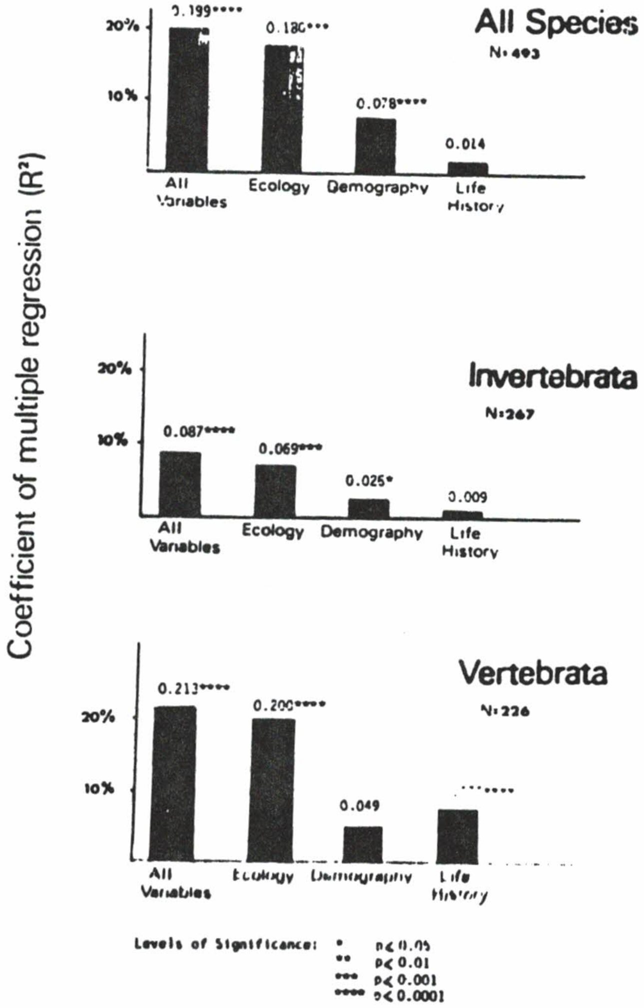
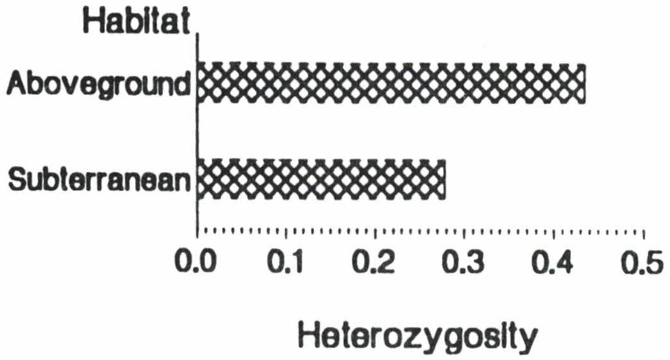


Figure 12: Levels of heterozygosity of 184 small mammalian species: aboveground versus subterranean (=fossorial + subterranean) [from Nevo et al, 1990].



Subterranean species include fossorials

and predictable by 3-4 variable combination of ecological, demographic and life history variables, largely in this order (Fig. 11). Ecological factors account for the highest proportion of the 20% explained genetic variance of all species as compared with demographic and life history factors (90%, 39% and 3.5%, respectively). Within individual higher taxa the explained portion of genetic diversity increased considerably (mean 44%, and maximum of 74% in molluscs). However, significant small intercorrelations (r = mostly 0.1-0.3) occur both within and between the subdivided biotic variables. Therefore, additional critical tests at the population micro-geographical levels, complemented by biological, biochemical and physiological experimentation, may verify the inferences of causal relationships between biotic factors and genetic diversity.

21.2.2 Salinity Stress and Isozymes

Salinity stress is one of the significant environmental stresses affecting life. For example, salinity was shown to account for about 70% of the losses in crop yield that can be attributed to abiotic stresses [Pasternak, 1982]. We have tested salt tolerance in the progenitors of cultivated cereals [Forster et al, 1990; Nevo et al, 1992a,b]. In preliminary outdoor experiments in the northern Negev desert, we first tested 21 and 11 populations of Hordeum spontaneum and Triticum dicoccoides, respectively, at low levels of salt stress (45, 60 and 120 mM). We then tested in a computerized greenhouse system, 5 selected populations of H. spontaneum from the Mediterranean Coastal Plain of Israel and northern Negev Desert, at 250 and 350 mM of NaCl; and 5 populations of T. dicoccoides, from the eastern steppes of Samaria, Mt. Hermon and Mt. Carmel, at 175 and 250 mM of NaCl. We found uniquely superior genotypes derived from the above selection of H. spontaneum ripening at 350 mM NaCl (=

Figure 13: Frequency distribution of the level of heterozygosity of 188 amphibian species [from Nevo and Beiles, 1991].

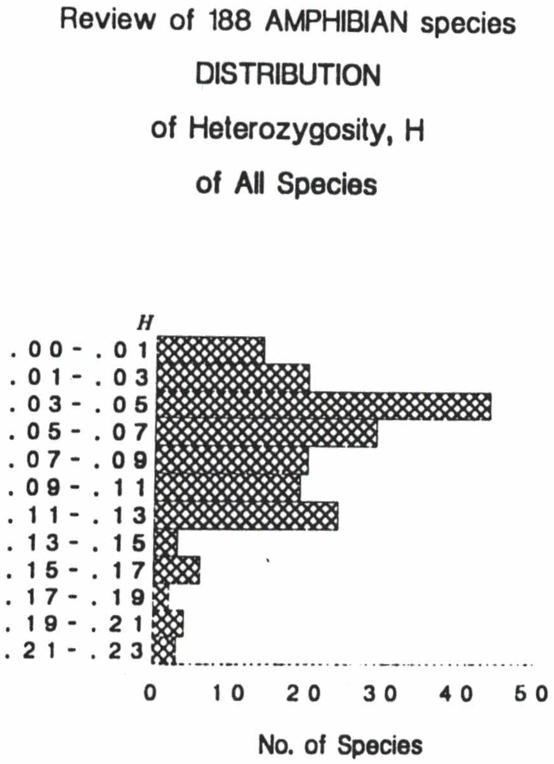
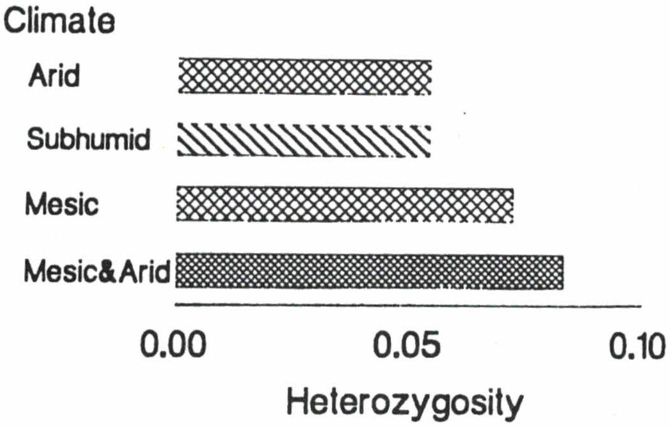


Figure 14: Levels of heterozygosity of 188 amphibian species according to their climatic regimes [from Nevo and Beiles, 1991].



60% sea water) and superior genotypes of T. dicoccoides ripening at 250 mM (= 40% sea water).

We also found widespread genetic polymorphism for 22Na uptake within and between populations of wild emmer wheat, T. dicoccoides in Israel, displaying salt tolerance resources for wheat improvement [Nevo et al, 1992a]. The xeric populations significantly displayed lower values of relative 22Na uptake as compared with mesic populations. Both ecological and isozyme markers, either singly or in combination, explain up to 81% of the variance in 22Na uptake. Thus, ecology and isozymes appear to be good guidelines for predicting the ecogeographical location and allozymic constitution of specific low relative 22Na uptake genotypes, which are presumably associated with high salt tolerance relevant to wheat improvement. We also outlined genetic strategies for improving the salt tolerance of wheat and barley, and located salt tolerance genes to specific wheat and barley chromosomes [Forster et al, 1990].

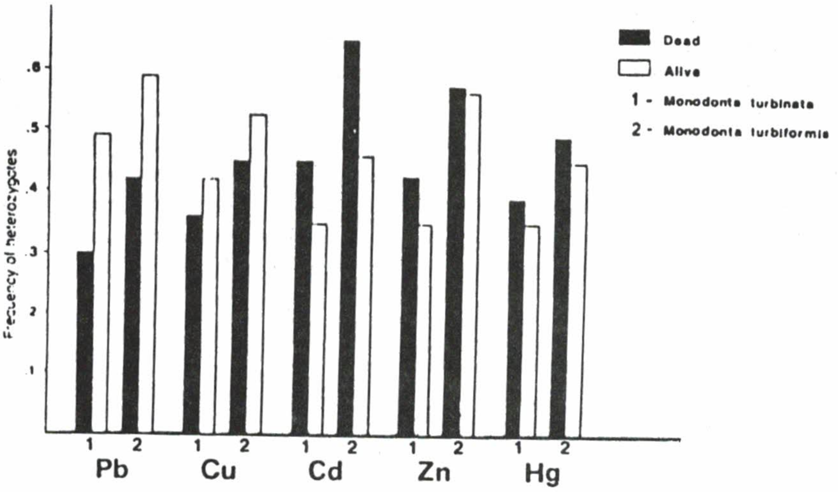
21.2.3 Thermal Stress and Isozymes

Temperature stress affects protein structure and function [Hochachka and Somero, 1984]. We have tested the effects of temperature stress on barnacle biodiversity, phenotypic and genotypic diversities. We showed dramatic changes on all of these factors [Nevo et al, 1977]. The test was conducted in the open Mediterranean sea water canals of the Haifa Electrical Plant Cooling system, where temperature seems to be the only environmental factor distinguishing the cool inflowing, from the nearby warmer outflowing canal (about 12°C and 9°C difference in summers 1975 and 1976, respectively).

Our results indicated that: (i) Balanus amphitrite decreased threefold in size, and fourfold in numbers, in the warmer canal. Similarly, repetitive trends indicated changes in allelic frequencies and in mean heterozygosity, H, which declined drastically from a mean = 0.111 in the cooler, to $H = 0.047$ ($p < 0.001$) in the narrower niche warmer canal. These results corroborate the niche width variation hypothesis which suggests a positive relation between the level of variation and niche breadth [Van Valen, 1965]. The relative fitness of aa as compared to AA morphotypes, in the warmer versus the cooler canal for malic enzyme (Me), acid phosphates (Acph), esterase-3 and esterase-8 (Est-3,8) was 3.6, 2.2, 21.3 and 4.4, respectively. Evidently, strong directional selection is operating in the warmer canal in favor of the four aa homozygotes, apparently because of their high thermal fitness. Furthermore, significant linkage disequilibria were found only in the warmer canal between Ao-3F-Est-8F ($D = 0.024$, $p < 0.001$) and Est-3F-Est-4F ($D = 0.021$, $p < 0.01$); and the genetic distance between the cooler and warmer canal was $D = 0.036$.

Similar trends in size, numbers, heterozygosity and allele frequencies in several loci were also detected in 1975 in B. eburneus, which coexists with B. amphitrite. However, the former temperate species was more sensitive than the latter subtropical species to the thermal stress, and totally disappeared from the warmer canal in 1976. Six out of seven enzymes showing differences between the cooler and warmer canals were either regulatory or variable-substrate enzymes. The former relate to metabolic regulation, the latter may affect metabolic rates. Our barnacle data strongly support the hypothesis that allelic isozymes are positively selected directly or indirectly by natural selection as adaptation to different thermal environments. Positive and/or negative Darwinian selection operated in this case both at the molecular (proteins) and organismal (size, numbers, species) levels.

Figure 15: Differential survivorship of heterozygotes of phosphoglucose isomerase (Pgi) of Monodonta turbinata and M. turbiformis in five pollutants [from Nevo et al, 1983b].



21.2.4 Chemical Stress and Isozymes

We have studied chemical stresses at two levels: (i) Pollution resistance of allozyme polymorphisms in marine organisms to inorganic and organic pollutants [Nevo, 1986b; Nevo et al, 1983b], and (ii) genetic response to herbicide spraying and allozyme predictability of herbicide resistance [Snape et al, 1991a,b; Nevo et al, 1992c].

21.2.4.1 Marine Pollution Stress

We have demonstrated both in the sea [Nevo et al, 1978] and the laboratory, under controlled experiments, that isozyme diversity is not neutral but is very sensitive to pollutant stress [Nevo, 1986b; Nevo et al, 1983b, 1987; Lavie and Nevo, 1986a,b 1987, 1988; Nevo and Lavie, 1989a,b] (Fig. 15). These studies clearly illustrate the following results for allelic isozyme polymorphisms: (i) They are very sensitive to environmental pollution of inorganic and organic pollutants, and display significant differential survivorship (or mortality) in laboratory experiments. This makes them excellent genetic monitors of marine pollution in nature [Nevo et al, 1984b, 1987]. (ii) They display different responses to single pollutants (e.g. mercury or cadmium), as compared to interacting pollutants, for example the effects of cadmium and mercury on marine gastropods [Lavie and Nevo, 1986a, 1987]. (iii) Isozymes display differential fitness at single [Nevo and Lavie, 1989a] and multilocus structures [Lavie and Nevo, 1986b, 1988]. (iv) Natural selection for resistance to mercury pollution was found in marine gastropods in nature [Baker et al, 1985]. The evolution of metal pollution tolerance in marine organisms may be as fast as that of metal tolerance in plants and the evolution of industrial melanism in moths. (v) Species of marine gastropods with broader ecological niches display higher genetic diversity and higher resistance to a battery of inorganic and organic pollutants, than narrow-niche species [Nevo et al, 1986e]. Thus, the fitness of marine organisms is positively correlated with heterozygosity supporting the niche-width variation hypothesis with regard to pollutants.

21.2.4.2 Herbicide Stress in Wild Emmer Wheat

Crop species can show differential responses to successful, widely used, herbicides where some varieties are unaffected by application, whilst others show symptoms of damage ranging from a slight reduction in vigor to complete plant death. The elucidation of the genetical control of such responses is important in developing strategies for breeding herbicide resistance in crop species. It is also useful in understanding the modes of action of the herbicides and the evolution of resistance in weed species [Snape et al, 1991a].

The responses of wild populations of wild emmer wheat, Triticum dicoccoides, from different ecogeographical areas of Israel, to three herbicides, difenzoquat, chlortoluron and metoxuron, which are commonly used on cultivated wheats, were studied [Snape et al, 1991b]. Although cultivated wheats are polymorphic for a response to difenzoquat, all families of populations of the wild species were resistant. The species was, however, polymorphic for response to both chlortoluron and metoxuron. In addition, there appeared to be differentiation among populations in the frequencies of resistant and susceptible morphs for these herbicides. There was also a close correspondence between the responses of individual families to chlortoluron and metoxuron, which suggests a common genetic control.

Herbicide response polymorphisms in wild emmer wheat can be predicted by both ecological factors and allelic isozyme markers [Nevo et al, 1992c]. We demonstrated that the scores and frequencies of chlortoluron (CT) and metoxuron (MX) resistance and susceptible phenotypes of wild emmer wheat, were correlated with ecological factors and allozyme markers. Some isozyme loci located on chromosome 6B (e.g. Adh, Est-4, Got and Amy-1), which also harbors the CT and MX resistance gene, provide good genetic markers for herbicide resistance breeding.

21.2.5 Biotic Stresses and Isozymes

Parasite and pathogen stresses are among the most influential environmental factors on the evolution of organisms [Haldane, 1949; Taylor and Muller, 1976; Anderson and May, 1982; Burdon, 1987; Wakelin and Blackwell, 1988], and on sex [Hamilton, 1991]. Our major studies concerning biotic stresses were conducted on wild cereals [Nevo, 1988b, 1992b] and on subterranean mole rats [Nevo and Beiles, 1992b] and will be detailed below.

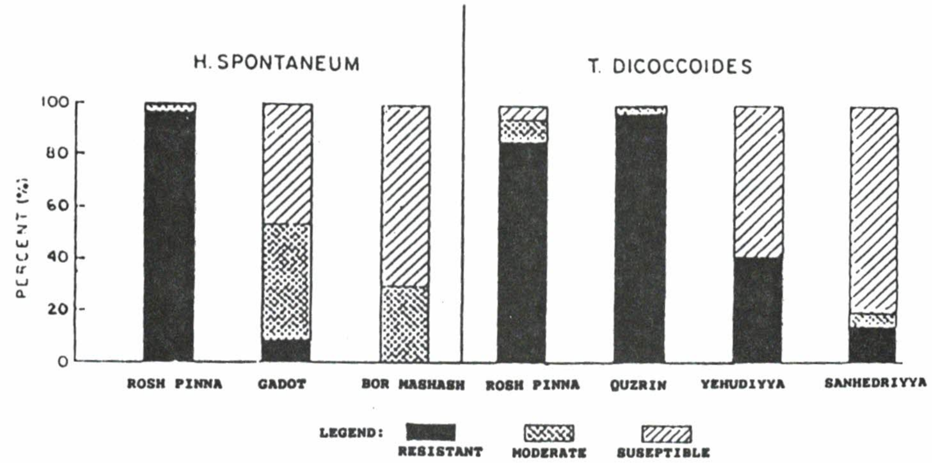
21.2.5.1 Disease Resistance in Wild Cereals

We studied disease resistance polymorphisms of powdery mildew in wild barley, Hordeum spontaneum [Moseman et al, 1983; Nevo et al, 1984c; Jana and Nevo, 1991] and in wild emmer wheat [Moseman et al, 1984, 1985; Nevo et al, 1985a] (Fig. 16). Likewise, we studied disease resistance polymorphisms against leaf rust in wild barley [Moseman et al, 1990; Jana and Nevo, 1991]; and leaf, stem and stripe (= yellow) rusts in wild emmer wheat [Moseman et al, 1985; Nevo et al, 1986c, 1991b; The‘ et al, 1992].

21.2.5.2 Selection for Mhc heterozygosity in mole rats

We have recently reported on selection for class II Mhc heterozygosity in subterranean mole rats [Nevo and Beiles, 1992b]. Mhc organization and polymorphism have previously been studied in the four chromosomal species of the Spalax ehrenbergi superspecies in Israel, serologically, and at the DNA, RFLP and sequence levels of class I and class II genes [Nevo and Klein, 1990]. We demonstrated that the observed heterozygosity of Mhc class II genes P¡1, with 11 alleles, and Q=, with at least 14 alleles, is positively and significantly correlated with infectivities of ectoparasites (gamasid mites) and endoparasites (helminths) (Fig. 17). Mhc

Figure 16: Polymorphism of resistance to Erysiphe graminis in populations of wild barley (Hordeum spontaneum) and of wild wheat (Triticum dicoccoides) in Israel [from Nevo, 1986a].



heterozygosity is highest in the most infected area, which is in the most humid-warm region of the superspecies range, or where two zoogeographic regions overlap. We concluded that the evolutionary forces responsible for the Mhc class II, two-gene polymorphisms, include selection for increased heterozygosity as a defense strategy against ecto- and endoparasite infections.

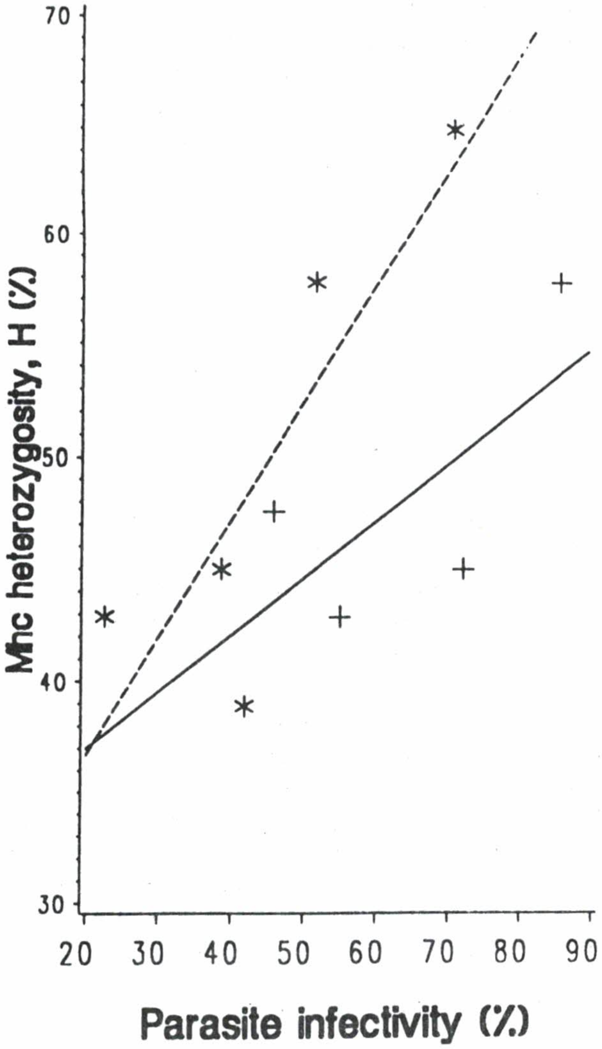
21.2.6 Isozymes as Genetic Markers

Linkage or association of genetic markers to quantitative traits of agronomic importance can substantially simplify the genetic analysis of complex quantitative traits [Korol et al, 1990]. Enzyme marker genes are ideal candidates for quantitative genetic analysis. We have recently applied this powerful methodology to the analysis of genetic resources of wild cereals in Israel, primarily wild emmer wheat, Triticum dicoccoides, and wild barley, Hordeum spontaneum, the progenitors of cultivated wheats and barley, respectively [reviewed in Nevo, 1987]. We have found that allelic isozyme markers and ecological factors provide an important predictive method for identifying elite genotypes characterized by single or multiple disease resistances [Nevo et al, 1984c, 1985a], high protein content [Nevo et al, 1985b, 1986d]; a variety of quantitative traits of agronomic importance including germination, earliness, biomass and yield variables [Nevo et al, 1984d,e]; photosynthetic yield [Nevo et al, 1991c]; herbicide resistance [Nevo et al, 1992c]. Our predictive methodology could be improved by additional crossing tests in an attempt to verify the results derived from the correlation analysis and thus establish the linkage relationships between the marker gene and the quantitative trait under discussion. This methodology, if further developed by additional isozyme and DNA markers, verified by crossing tests and gene mapping, could substantially contribute to the sampling and utilization of the genetic resources of wild gene pools for crop improvement.

21.3 Theory of Isozyme and DNA Polymorphisms in Nature

How Much of Genetic Diversity (Proteins and DNA) in Nature is Adaptive? The evidence presented here derived from local, regional and global studies of protein and DNA (both

Figure 17: Mhc heterozygosity as a function of gamasid mites and helminth infectivity. Dashed line and stars represent gamasid mites, and continuous lines and plus signs represent helminths [from Nevo and Beiles, 1992].



nuclear and mitochondrial) diversities, indicate a massive, nonrandom structure of genetic diversity in nature. This comprehensive evidence strongly suggests that the levels and differentiation of genetic diversity are primarily maintained and oriented by natural selection. While stochastic factors certainly interact with natural selection, the environmental patterns described here at all geographical scales, can not result from neutral and stochastic factors as the major architects of genetic diversity and differentiation. Likewise, it seems implausible that migration, which equalizes diversity, and mutation rates which are too weak to be recognized, are the main determinants of this massive structuring of genetic diversity. Natural selection in its various forms, appears to be the major architect of evolution, not only at the phenotypic but most importantly at the genotypic level [Nevo, 1988a,b]. Several selection theories, discussed in Nevo [1988b], advance predictions supported by the evidence reviewed here. These involve the following theories: (i) selection-balance; (ii) selection- migration; (iii) multilocus; and (iv) sexuality.

21.4 Conclusions and Prospects

The conclusion that natural selection is the major evolutionary force maintaining and orienting molecular evolution, was documented and cited above and is summarized below:

1. Ecological Factors

    - Genetic diversity in nature is ordered and structured on a massive scale, rather than representing chaos (Figs. 3,9,10,12).
    - Genetic parallelism predominates across unrelated taxa sharing similar ecologies, across all geographical scales. Generally, the level of genetic diversity is positively correlated with niche breadth, supporting the niche width-genetic variation hypothesis (Figs. 1,5,6,7,10,12,14).
    - Ecological-genetic correlations predominate in nature. Ecological factors appear to be the main predictors of genetic diversity and divergence across phylogeny at all geographical scales: local, regional and global (Figs. 2,5,6,7,10,11). Environmental ranges and stresses appear to be major determinants of the levels and differentiation of genetic diversity, and of the mechanisms generating it, such as recombination [Korol et al, 1990], among others. We have tested the following stresses: A. Abiotic: (i) climatic; (ii) salinity; (iii) thermal; (iv) chemical (inorganic and organic); and B. Biotic: (v) parasites and pathogens.

2. Laboratory Experiments and the Nature of Isozymes

    - Differential survivorship of allelic isozyme genotypes, caused by controlled laboratory pollution stress experiments (Fig. 15), negate the idea that isozyme polymorphisms are neutral.
    - Differential biochemical kinetics of allelic isozyme genotypes [reviewed for the early literature in Nevo, 1983b] in diverse environmental conditions, suggest that they contribute to the fitness of organisms.

3. Evolutionary Forces in nature

    - Genetic drift. Genetic polymorphisms of protein and DNA, as well as phenotypic diversities in very small and isolated populations (e.g. isolates of mole rats in the Israeli Negev Desert, N= around 100 [Nevo, 1989b] negate genetic drift as a major independent evolutionary force affecting genetic differentiation.

- Migration is excluded in several studies, such as in mole rats and wild cereals, as a major evolutionary force affecting genetic differentiation. The discovery of environmentally-structured genetic diversity in spite of existing migration suggests a secondary role of migration in large scale spatial differentiation. This is verified in autocorrelation analyses [e.g., Nevo and Beiles, 1989].

- Mutation rates are very low to counterbalance selection and migration, hence can not provide a major role in orienting evolution as suggested by Ohta [1974]. Mutation pressure can only counterbalance genetic drift in very large populations. Mutability (and certainly recombination [Korol et al, 1990]) can provide the raw material for positive selection, regardless of its low rate. Likewise, many genetic polymorphisms in nature are old, predating speciation and evolutionary divergences (cladogenosis). These facts suggest that the role of mutability in orienting evolutionary change is secondary at best.

Natural selection at the molecular and organismal levels, appears to be the major evolutionary force maintaining and orienting genetic diversity and differentiation, i.e. the evolutionary process in nature. Natural selection is multifaceted including diverse frequency-dependent, balancing and epistatic phenomena. Diversifying selection in heterogeneous environments appears to be an important vehicle of evolutionary genetic change, beside other modes such as heterosis. Noteworthy, selection operates on phenotypes. However, at the molecular level its effects can be observed not only on single genes, but most importantly on two-locus (gametic phase disequilibria) and multilocus structures as well as genome organization, in both inbreeders and outbreeders.

Natural selection operates on genotypes through their phenotypic appearance. The dualism of the neutral theory of molecular evolution [Kimura, 1983] suggesting primarily the operation of natural selection at the phenotypic level and neutrality, or near neutrality, at the genotypic level, is unnatural and unnecessary, since it is not supported by current evidence from genetic polymorphism in nature.

Critical experiments, in nature and the laboratory across phylogeny, geography, ecology, demography and life history spectra, are still very much needed to elucidate the mode, tempo and diverse facets of selection. Natural selection may be operating not only on individual phenotypes but on groups such as demes, populations, species, ecosystems and whole biota. The global and extensive experiment of domestication by man strongly suggests the tremendous potentials, of genetic diversity existing in nature as a raw material for selection. However, the modes, patterns and stages of the operation of natural selection are largely unknown in details.

Evolutionary theory is still in a constant change and improvement as is the evolutionary process itself. However, its foundations substantiated by the productive bridge between Darwinism and classical as well as modern genetics are the main promising guidelines for its future development. The selection of heritable diversity at the genotypic and phenotypic levels due to changing environments over space and time remain as solid as ever. Adaptation to external and internal environments, at both the molecular and organismal levels, appears to remain, despite all other interacting mechanisms, the core of evolutionary change over space and time.

21.5 Summary

The evolutionary significance of genetic diversity in natural populations of plants and animals, based on studies conducted during 15 years, 1977-1992 at the Institute of Evoltuion, University of Haifa, Israel, was reviewed. We used the ecological-genetic correlation methodology at three geographic levels: (1) local: several species of wild cereals, landsnails, and barnacles in Israel: (2) regional: 38 species in Israel; of these, 21 range from the Mediterranean region to the Negev Desert; also included were two species of wild cereals in the Near East Fertile Crescent; and (3) global: (a) 1111 species of animals and plants ranging worldwide; (b) 184 subterranean mammalian species; and (c) 188 amphibian species across the planet. The species involved in these local, regional and global analyses are largely taxonomically unrelated. They vary in their ecologies, demographies, life histories, and other biological variables. The response of these species were analyzed to environmental ranges (niche-width) and the following stresses: A. Abiotic: (i) aridity, (ii) salinity, (iii) thermal, (iv) chemical, and B. Biotic: (v) pathogens and parasites. They were mostly tested for allozymic diversity by routine horizontal starch gel electrophoresis at 25 gene loci on average (range 14-50 loci). In addition, several studies were reviewed on nuclear and mitochondrial DNA polymorphisms in animals and plants in Israel.

The following results were found at all three geographic levels: (1) the levels of genetic diversity vary nonrandomly among genes, populations, species, and higher taxa; and (2) genetic diversity at single and multilocus structures as well as genome organization are partly correlated with, and predictable, primarily by ecological factors. These results corroborate the adaptive, environmental theory of genetic diversity, and they were confirmed for several allozyme loci in controlled laboratory experiments on pollution biology. The genetic patterns obtained are inconsistent with the neutral theory of molecular evolution. By contrast, natural selection in its various forms appears to be a major differentiating and orienting force of evolutionary change at the molecular level of protein and DNA polymorphisms.

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