

# Sudden Origins: A General Mechanism of Evolution Based on Stress Protein Concentration and Rapid Environmental Change

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A major theme in Darwinian evolutionary theory is that novelty arises through a process in which organisms and their features are gradually transformed. Morgan provided Darwinism and the evolutionary synthesis with the idea that minor mutations produce the minuscule morphological variations on which natural selection then acts, and that, although mutation is random, once a process of gradual genetic modification begins, it becomes directional and leads to morphological, and consequently organismal, transformation. In contrast, studies on the role of cell membrane physical states in regulating the expression of stress proteins in response to environmental shifts indicate the existence of a downstream mechanism that prevents or corrects genetic change (i.e., maintains “DNA homeostasis”). However, episodic spikes in various kinds of environmental stress that exceed an organism’s cells’ thresholds for expression of proper amounts of stress proteins responsible for protein folding (including stochastically occurring DNA repair) may increase mutation rate and genetic change, which in turn will alter the pattern of gene expression during development. If severe stress disrupts DNA homeostasis during meiosis (gametogenesis), this could allow for the appearance of significant mutational events that would otherwise be corrected or suppressed. In evolutionary terms, extreme spikes in environmental stress make possible the emergence of new genetic and consequent developmental and epigenetic networks, and thus also the emergence of potentially new morphological traits, without invoking geographic or other isolating mechanisms. *Anat Rec (Part B: New Anat) 289B:38–46, 2006.*

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## INTRODUCTION

When Darwin (1859) proposed his model of gradual evolution, he, like other evolutionists, was unaware of the DNA/chromosomal organization underlying the behaviors and morphologies he discussed. His model of inheritance (pangenes) combined theories of selection, blending inheri-

tance, and use-disuse (inheritance of acquired characteristics) (Darwin, 1868). Contemporary anatomists, however, such as Huxley (1863) and especially Mivart (1871), eschewed a model of gradual transformation, favoring instead a developmentally based, saltational explanation for the origin of novel features. Early geneticists (de Vries, 1910) did not embrace

gradualism and continuous variation because Mendelism emphasized discontinuous variation, which was more compatible with saltational origins of novelty. Morgan (1903) initially rejected both Mendelism and Darwinism—like de Vries, seeing Darwinism as explaining the origin of adaptation, not species—but later melded the two “isms” as neo-Darwinism (Morgan, 1925). Although observing major morphological changes in *Drosophila* mutants (e.g., eyeless, apterous, bithorax), Morgan focused only on minor variation (e.g., eye color, wing length, thoracic bristle number), which he believed result from small mutations that lead to continuous variation across, and transformation of, species. Mayr (1942) expanded on this idea: geographically isolated subspecies become true species by accumulating minor genetic changes that eventually lead to repro-

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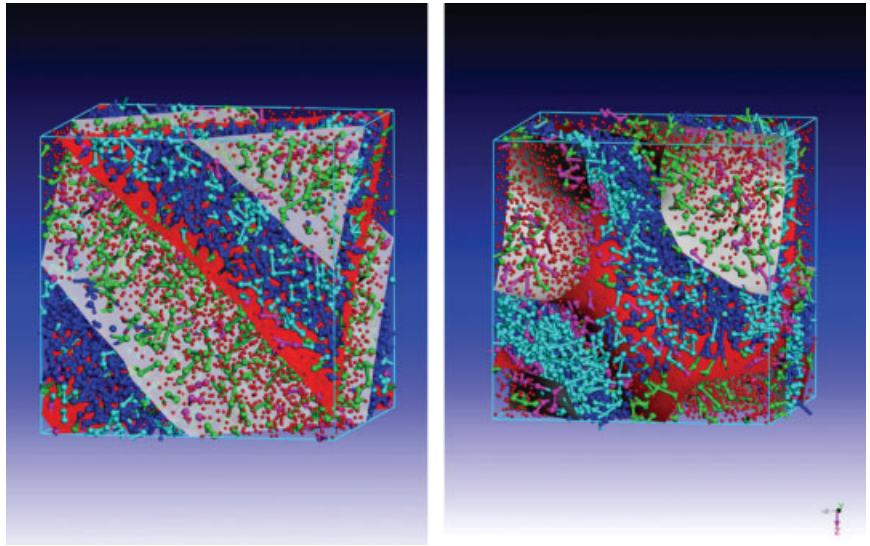
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ductive incompatibility. Nowhere, however, in these or subsequent formulations of evolutionary change resulting from accumulated genetic modification is the cellular “target” of inferred mutation identified. Nevertheless, whatever its source, mutation can affect any cell in the body, of which the vast majority are somatic. Thus, the only time at which any mutation can have a hereditary and potential evolutionary effect is during meiosis.

Implicit in Darwinian models is the notion that organisms constantly change, genetically and morphologically [even though the tempo of change may not always be gradual (Simpson, 1944; Eldredge and Gould, 1972)]. Nevertheless, intermediates between living pro- and eukaryotes do not exist, variation within species reflects fluctuating frequencies of existing features, and the fossil record does not document seamless transformation of lineages. Although the fact of gene-expression differences might be fitted to a model of gradual change, such an inference is inappropriate. For example, since the origin of Metazoa, the number of classes of regulatory genes remained stable, while new genomic structure and modes of transcriptional regulation appeared (Levine and Tjian, 2003): e.g., exon shuffling (splicing), different regulatory pathways, enhancers, silencers, and complex chromatin organization. Thus, in contrast to the yeast genome with about 300 transcription factors, the *Drosophila* genome contains more than 1,000, while the human genome may only have around 3,000 (Wyrick and Young, 2002). Thus, genomic diversity and organismal complexity likely emerged along with more elaborate mechanisms for the regulation of gene expression.

Alternate splicing of exon-containing genes permits a single gene to code for different proteins. For example, in vertebrates, mRNA splicing allows sound-sensing inner ear cells to detect frequencies from ca. 50 to 5,000 Hz because the *Slo* gene and three *neurexin* genes, which encode proteins that may act as synaptic cell surface receptors or cell-adhesion molecules, can generate, respectively, more than 500 and potentially up to



**Figure 1.** Molecular dynamic simulation of lipid membrane. Stress induces a transition from lamellar (A) to cubic organization (B), disrupting membrane organization (data not shown).

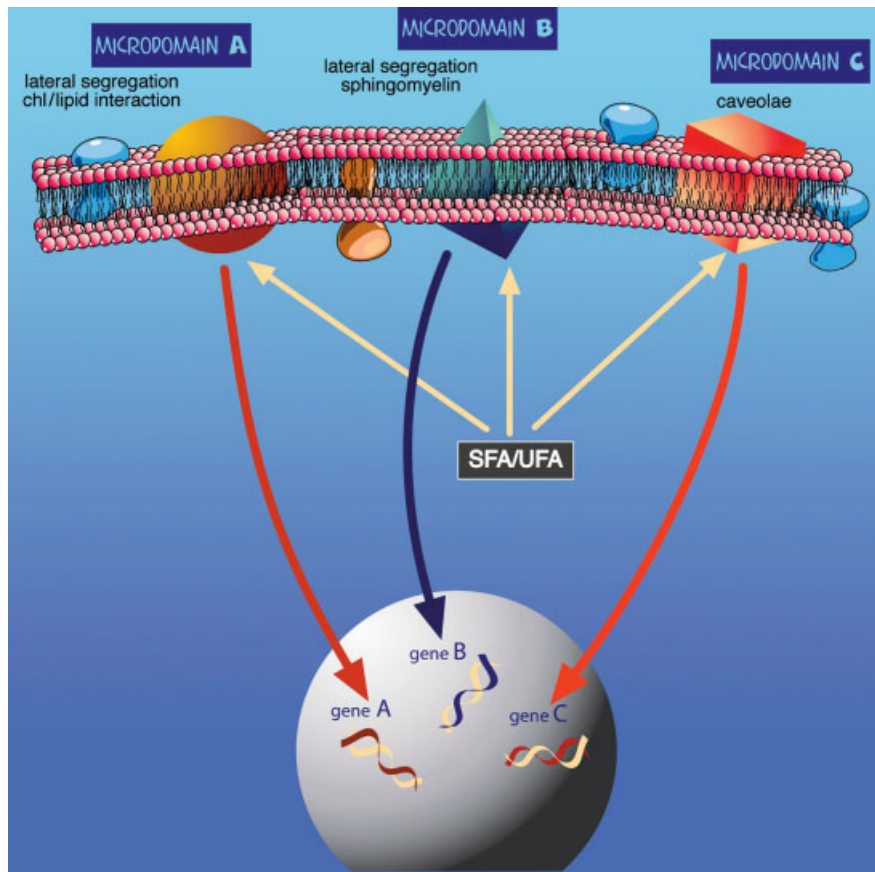
2,000 alternatively spliced forms (Rosenblatt et al., 1997). In *Drosophila*, the axon-guidance receptor gene, *Dscam*, which contains 95 alternatively spliced exons, may produce over 38,000 protein isoforms: almost three times the entire *Drosophila* genome (Maniatis and Tasic, 2002).

Four decades of research on physical and biological stresses have identified a class of proteins called stress or heat shock proteins (HSPs), which are coded by stress or heat shock genes (HS). Although first identified in experiments in which heat (temperature) was the stress inducer, it has since been found that HSPs are not only fundamental under a variety of stress conditions [such as drought, salinity, and wind (Hazel and Williams, 1990; Vigh et al., 1998; Hartl and Hayer-Hartl, 2002; Goldberg, 2003)] but also key to basic cellular processes such as protein folding, translocation, splicing, membrane stabilization, nucleic acid and protein synthesis, spliceosome protection, chloroplast photosynthesis, and hyperfluid membrane physical state (MPS) compensation (Vigh et al., 1998; Nollen and Morimoto, 2002; Tsvetkova et al., 2002)]. Recent research has focused on mechanisms by which cells perceive stress via a primary sensor that translates it into signal cascades that activate HS mRNA transcription (Vigh et al., 1998, 2006; Vigh and Maresca, 2002). Different laboratories have shown that preexisting lipid composition and the

physical state of the membrane determine the extent of HS gene-induced damage to membranes (Carratù et al., 1996; Horvath et al., 1998). Thus, the cell membrane translates abrupt changes in extracellular physical conditions into intracellular responses that are coupled with stress response (Helmreich, 2003; Török et al., 2003). Such a mechanism of sensing physical stresses applies also to biological signals through G-protein-coupled receptors, which are finely tuned membrane lipids, and MPS. Further, the membrane nonlamellar-phase propensity cubic organization (Fig. 1) is involved in the interaction of certain amphitropic proteins (G-proteins and protein kinase C) with membranes (Escribá et al., 1995, 1997), thus controlling gene expression (Fig. 2).

## MOLECULAR AND MORPHOLOGICAL CONTRADICTION

Current evolutionary theory assumes various molecular phenomena. For instance, under a constant mutation rate, new phenotypes should emerge gradually, because, as Morgan (1916) argued, the chance of a mutation affecting a trait would be increased by an earlier mutation affecting the same trait. Although not demonstrating this experimentally, Morgan (1916) believed that evolution proceeds via the accumulation of small mutations that gradually “push” phenotypic change in a particu-



**Figure 2.** Model of membrane domains in regulating the expression of specific genes.

lar direction. But the premise that one mutation can increase the likelihood of another following it along similar lines is contradicted by the random nature and statistically insignificant probability of mutation. Morgan's experiments also did not produce new phenotypes; they only manipulated the frequency of extant *Drosophila* variants. Thus, the early genetic rationale for gradual evolutionary change, which ultimately informed the evolutionary synthesis, was not grounded in fact (Schwartz, 1999a). In addition, many of Morgan's (Morgan et al., 1926) observations record the loss, not acquisition, of phenotypic properties (e.g., the eyeless mutant in *Drosophila*). Other observations that may appear profound do not represent the introduction of new genetic material, e.g., the bithorax mutant. Mutation in the *Ubx* gene may cause duplication of a segment in the *Drosophila* embryo (Duncan, 1996), but this does not demonstrate how the original single pair of wings and associated structures emerged.

Since a commonly assumed mecha-

nism underlying morphological change is point mutation (a simple event statistically), the time required to produce change should be predictable because mutational events occur with a known and constant (although low) frequency. Thus, if new genetic material arising via regularly occurring but rare mutation events accumulates, species transformation should also occur at a constant and predictable rate. Yet the metazoan fossil record shows the opposite: the sudden appearance of fully developed, major morphological novelties (i.e., bony skeletons, jaws and teeth, limbs with zeugopods) in many different kinds of animals, as well as of different kinds of animals (e.g., insects) (Schwartz, 1999a, 1999b). The same is true with regard to the origin of different kinds of plants as well as their parts (Niklas et al., 1983; Willis and McElwain, 2002). As such, we might seek an underlying mechanism for producing morphological novelty that involves more complex series of events requiring the acquisition and proper regulation of new genetic material in both the animal and plant kingdoms.

## EXPERIMENTAL EVIDENCE

Cell membrane physical state or MPS is described as the tolerance of the architecture of the membrane to constant dynamic restructuring of molecular- and higher-level domains under environmental change and their continuous feedback with DNA (Tsvetkova et al., 2002; Török et al., 2003; Vigh et al., 2006). Membrane fluidity [i.e., saturated/unsaturated fatty acid (SFA/UFA) and/or membrane-protein/lipid ratios] is controlled in both animals and plants by environmental temperature and/or diet (Ntambi, 1992; Logue et al., 2000; Hochachka and Somero, 2002). Organisms produce mono-UFAs by the activity of desaturase enzymes that introduce double bonds at specific positions in SFAs (Stukey et al., 1990). A decrease in ambient temperature causes an increase in the synthesis of UFAs that then modify the MPS by introducing double bonds in specific positions in the SFA to form a corresponding UFA (e.g., 18:0 stearic acid is transformed into a 18:1 oleic acid); increases in temperature lead to higher levels of SFA. Because of this membrane property, organisms can cope with normal temperature or other environmental variations in their own regions, but cannot adjust to rapid drastic environmental change.

## ROLE OF HEAT SHOCK PROTEINS

With regard to temperature, complex eukaryotes and plants adapt to gradual changes often in less than 2 months (Hazel and Williams, 1990; Hazel, 1995). But if temperature change occurs within seconds or minutes, cells respond with a different and more rapid mechanism, of which the best known is the heat shock response (HSR). HSR is a cell's temporary reaction to sudden stress. HSPs constitutively present under physiological conditions properly fold proteins as they are synthesized (i.e., HSPs are molecular chaperones). Under HS conditions—typically 5–7°C above an organism's physiological temperature—a heat shock factor (HSF) trimerizes and positively activates HS mRNA transcription (Nollen and Morimoto, 2002). However, the



optimal temperature thresholds of HS gene transcription are determined not genetically, but by the physiological temperature(s) that organisms experience (Dietz and Somero, 1992).

Genetic modification of pro- and eukaryotic cells with a gene (e.g., fatty acid desaturase) whose product alters MPS also resets the threshold of HS gene transcription (Carratù et al., 1996; Horvath et al., 1998; Vigh and Maresca, 2002; Vigh et al., 2006). Since MPS depends on membrane lipid composition, and ambient temperature affects lipid synthesis, the optimal temperature of HSR is related to the MPS at the time of stress. Regions of membranes (rafts or membrane domains) under HS become hyperfluid by changing from a bilayer to a nonbilayer state (Vigh et al., 2006). While organisms have temperature regimes that allow them to tolerate and adapt to the temperature ranges where they live, members of the same species will respond somewhat differently to the same temperature fluctuations.

## A MODEL OF EVOLUTION

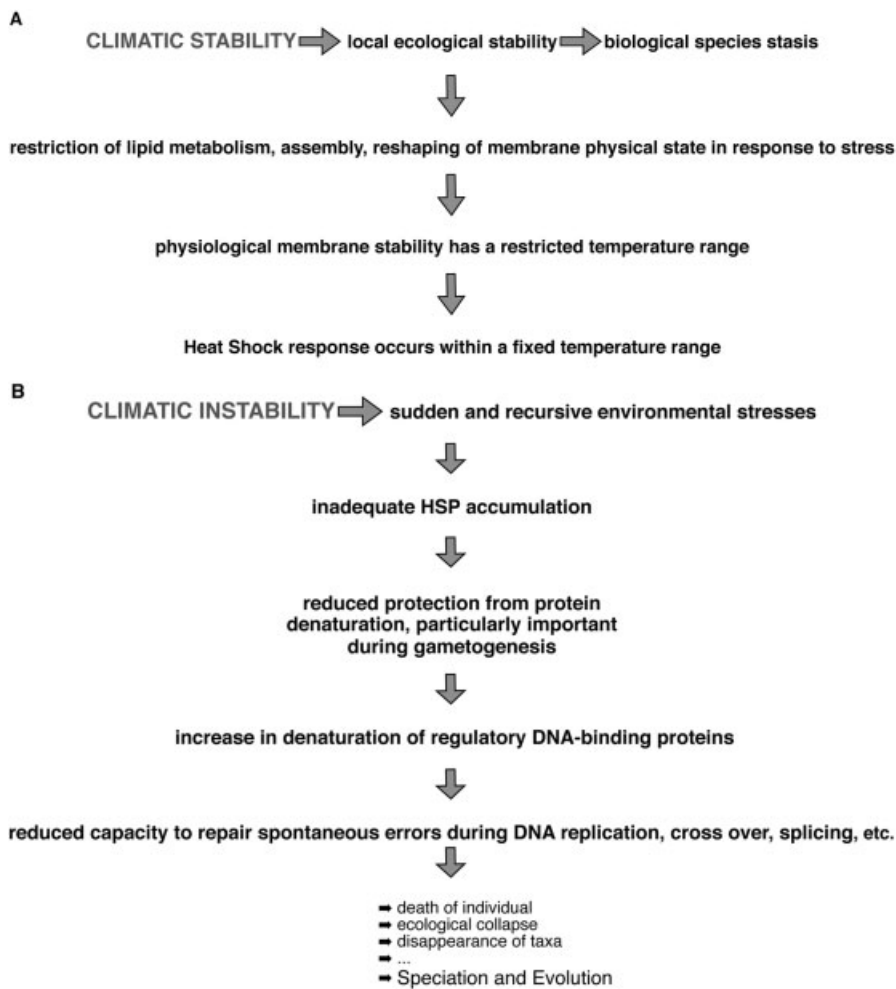
Frequency of mutation is a physical phenomenon that depends on the structure and mechanism of DNA replication, which is altered only by exposure to physical and chemical mutagens. Detectable mutation is the result of both a base substitution in a DNA sequence and an effective repair mechanism (a compromise between low and high efficiency of repair) that brings it to a fixed, constant, and very low rate of change (e.g., in Metazoa, it is ca. 1–10 nucleotides/generation, with genome sizes ranging from  $10^8$  to  $3 \times 10^9$  bp; in each of the  $10$ – $50 \times 10^{12}$  cells of the human body,  $10^4$ – $10^6$  DNA damages/day would occur without repair mechanisms) (Drake et al., 1998). If numerous mutational events occur during DNA replication, the system loses genetic information. Yet organisms whose cells have too efficient repair mechanisms could not cope with, or adjust to, changes in the physical and biological world. Thus, the tendency toward maintaining genomic stability conflicts with the actual episodic emergence of diverse morphological novelty. Can we explain this paradox?

The presence or absence of HSPs influences almost every aspect of reproduction. HSPs are among the first proteins produced during gametogenesis and early embryonic development. In a mouse embryo culture model, antibodies against HSPs impaired development at unique and specific stages (Neuer et al., 1997). A variety of Hsp70s are expressed from the time of zygotic gene activation in cleavage-stage embryos, through blastulation, implantation, gastrulation, neurulation, organogenesis, and on throughout fetal maturation (Luft and Dix, 1999). Proper reproduction depends on the accurate transmission of genetic information, which requires not only extreme accuracy of DNA replication and precise chromosome distribution, but also the ability to repair DNA damage and minimize the number of heritable mutations. Cells have evolved mechanisms that monitor, for example, chromosome structure and coordinate repair and cell cycle progression. DNA damage induces a number of signaling pathways that can cause cell cycle arrest and apoptosis or alter transcription and eventually DNA-repair mechanisms (Bin-Bing et al., 2000). Normally, repair mechanisms provide genomic stability (Smirnova and Klein, 2003; Pandita et al., 2004). But if they are drastically impaired (e.g., by physical stresses), the number of mutational events that occur and persist in the DNA increases substantially (Pandita et al., 2004). Obviously, the consequences of these events would be significantly different depending on whether they occur during meiosis or mitosis.

Both the efficiency of specific proteins involved in the accurate replication of DNA and the proper expression of genes in time and space depend on proper folding that confers the appropriate structural conformation and enzymatic activity required for protein-protein, DNA-protein, and protein-lipid interaction. Especially under stressful conditions, molecular chaperones also implement proper protein folding. Since organisms cope with stress within their normal physiological ranges because stress genes are transcriptionally activated by changes in MPS, the temperature threshold of HS gene activation is a

consequence of a specific MPS when environmental conditions are relatively stable (Fig. 3A). But if environmental stress exceeds the threshold of the normal HSR, the organism dies also because its genome cannot be structurally and transcriptionally protected by HSPs. Such stresses would include extreme spikes in temperature, major and prolonged episodes of temperature change, catastrophic tectonically or weather-related events (e.g., volcanisms, earthquakes, tsunamis, hurricanes, floods, tornados), drought, wind, asteroid impacts, and the effects of human activity, such as nuclear testing, chemical warfare, thermal pollution, overfarming (e.g., depleting top soil, overfertilization, and runoff), deforestation, power plant or sewage processing outflows, or possibly even black-body radiation, as well as the lack of response to natural or man-made disasters that affecting artificially reconfigured landscapes. Some stressors, such as sewage processing outflows, would be more geographically constrained. Other stressors, such as asteroid impacts, would initially be local but have the possibility of a cascading wider effect due to spreading atmospheric effects (e.g., wind and/or dust and thus black-body radiation). Clearly, some of the sources of stress we list above could be enacted simultaneously (e.g., wind resulting from or part of any number of factors).

Disappearance of taxa may be the result of what is called extinction, but the causes of extinction are not uniform: some individuals die because they cannot cope with severe change, while others die because their survival is tied to disappearing taxa. Some individuals may, however, survive because, even with a compromised ability to cope with severe change, their capacity to induce HSR is partially affected, which results in much lower amounts of HSPs during stress. If a stress-induced reduction in stress protein concentration occurs during meiosis and the production of gametes, the result could be evolutionarily significant. The lower amount of HSPs will stochastically affect the capacity to provide or restore proper folding to cell proteins (e.g., those responsible for the transcriptional regulation of developmental genes, DNA rearrange-



**Figure 3.** Schematic representation of cell and heat shock response under relatively normal stable (A) and unstable (B) climatic conditions. T, temperature.

ments, crossover, gene duplication, alternate mRNA splicing, and other crucial events and/or processes). Importantly, proteins involved in DNA-repair mechanisms will no longer be able to suppress naturally occurring mutations with their typical level of efficiency. Thus, while the frequency of base substitution or gene exchange is a physical parameter not directly affected by stress, impairment of the efficacy of the repair mechanism by an insufficient amount of HSPs will increase the number of persistent mutations (that is, increase the effective mutation rate). Further, stress during gametogenesis (Bowler, 1972; Dix, 1997) will affect males and females differently, not only because the details of this process differ between the sexes, but also because of other biological and physiological differences in their reproductive systems [e.g., as in mammals, where testicular HS

threshold may be lower than in other tissues (Sarge, 1995)].

Reduced synthesis of molecular chaperones will also stochastically affect the folding both of regulatory proteins responsible for the proper expression of developmentally regulated genes and of proteins involved, e.g., in chromosome rearrangement and DNA repair. This would further increase the number of retained, but normally suppressed or corrected, mutational events (again, increasing the effective mutation rate), without changing the actual rate of mutation (Fig. 3B). Of course, altered proteins controlling developmental genes only have potential evolutionary significance if they occur in gametes without affecting their viability and fertility. But since, as pointed out by Bateson (1913) and demonstrated by Morgan (1916), it is likely that the “mutation” (i.e., the availability of new signaling

pathways) will arise in the “recessive state” (i.e., be inactive), the potential for change will have no effect on its bearer or those descendants that inherit it (Haldane, 1932; Wright, 1932, 1940; Fisher, 1958; Schwartz, 1999a, 1999b). Inbreeding, which occurs in natural populations because individuals tend to find mates nearby, will enhance the rate at which recessives spread from one generation to the next, increasing the probability of producing homozygotes for the recessive state (Haldane, 1932; Wright, 1932, 1940; Schwartz, 1999a).

If extreme stress-induced major mutational events are brought together in the zygote in a homozygous state, the organism will probably die because the new condition will most likely interfere with genetic and consequent developmental and epigenetic constraints. Nonetheless, the fortuitous combination of mutational events affecting the regulation of development (including, for example, signaling pathways or morphogenetic gradients, as well as the physical consequences of cell size and packaging and other potential epigenetic factors) may on (rare) occasions result in morphological novelty that does not interfere with an organism’s survival. Thus, while it may take some number of generations for the recessive state to spread from the initial bearer of it, the novelty itself, whether lethal or viable, will emerge suddenly and in more than one individual (Schwartz, 1999a, 1999b). The number of individuals with novelties will increase as heterozygotic parents continue to produce homozygous offspring and as homozygotes mate with each other (Schwartz, 1999a, 1999b). Thus, the degree of genetic novelty that could occur in one individual would spread silently across a succession of generations in a relatively short period of time, eventually leading to a seemingly “instantaneous” appearance of morphological novelty in a number of individuals.

## INITIAL SUPPORT FOR THE MODEL

Studies on developmental abnormalities produced by stress both during embryogenesis and during differentiation (phenocopies) (Welte et al., 1995; Roberts and Feder, 1999) provide tangential support for this hy-

pothesis. All organisms induce a stress response, but there are specific stages during embryogenesis (e.g., the *Drosophila* blastoderm) when, under stress, HS genes are not transcribed and thus HSPs do not accumulate. For example, in *Drosophila*, even though *hsp83* is developmentally regulated under normal conditions, it is not induced at an HS temperature above 37°C (Arbona et al., 1993).

Petersen and Mitchell (1987) induced phenocopies in heterozygotes by heat shock [e.g., at 40.8°C, a multiple wing-hair phenocopy in the mutant *Drosophila* heterozygote (mwh/+)] and also demonstrated that the induction of thermotolerance that permits a moderate accumulation of HSPs in a nonlethal HS condition prevents heat induction of the multiple wing-hair and other phenocopies. Different kinds of embryological defects are produced in organisms depending on the exact timing of the stress (e.g., chicks with different numbers of wings, plants with different leaf morphologies, and mice and humans with brain abnormalities). The defect induced by environmental stress depends on the genetic background of the plant or animal as well as the type and extent of the insult.

The consistency with which these defects emerge under similar stressful conditions across different taxa supports the idea that, during embryogenesis, HSPs play a general role in the protection of developmentally regulated genes even though the DNA sequences involved in the development of these distinctly different organisms are totally unrelated. It is therefore likely that a primary function of HSPs is to confer proper folding to those proteins that control the correct timing and sequence of gene expression, especially during embryogenesis, when specific genes are expressed at high rates. Conversely, a reduction in HSP concentration during embryogenesis may lead to abnormal development and phenocopies. But it is precisely because this alteration occurs in somatic cells during embryogenesis that it is not inherited by the next generation.

HS and other environmental stresses that can induce HS response (e.g., drought, salinity, and wind) all affect MPS and protein denaturation

(Hazel and Williams, 1990; Vigh et al., 1998; Hartl and Hayer-Hartl, 2002; Goldberg, 2003). Diet and hormones influence lipid metabolism, inducing a change in the gel-to-fluid phase transition of the lipid phase of membranes and thus in HSR (Carratelli et al., 1996). Many membrane-fluidizing agents (e.g., benzyl alcohol, heptanol) alter HS gene transcription by changing the membrane lipid phase and MPS (Vigh et al., 1998), thus recalling Waddington's (1957) experiments, in which *Drosophila* phenocopies were produced when embryos were exposed to ether, which interferes with MPS and therefore with the heat shock response.

### THEORIES OF RAPID EVOLUTIONARY CHANGE

Saltationist theories of organismal change and speciation are not new (Mivart, 1871). De Vries (1910) based his mutation theory ("intracellular pangenesis") on the emergence of "mutants" or "monsters" in a single generation of evening primrose and snapdragon. Bateson (1894) and later Goldschmidt (1940) argued that novelty arises abruptly when development is altered. For Goldschmidt, minor mutations ("micromutations") are relevant to species' survival ("microevolution"), while "macromutations," which cause the larger-scale changes that produce species ("macroevolution"), result from chromosomal rearrangement. Dobzhansky (1941) and Mayr (1942) harshly criticized Goldschmidt for suggesting that macromutation-based novelty would be embodied in a single individual, a "hopeful monster."

Since Eldredge and Gould's (1972) original presentation of the model of punctuated equilibria was based on Darwinian natural selection and adaptation, but with rapid bursts of speciation, "hopeful monsters" were not an issue. But when Gould and Eldredge (1977) proposed that changes in regulatory genes, rather than an accumulation of minor mutations in structural genes, could produce new species, the model required a new mechanism to explain how more than one individual would have the regulatory change-induced morphological novelty. Population geneticists (e.g.,

Charlesworth et al., 1982) rejected Gould and Eldredge's suggestion on the grounds that their model adequately described (Darwinian) evolutionary change.

Historically, evolutionary theories have focused almost exclusively on animals. The model of punctuated evolution proposed by Eldredge and Gould (1972) suggested that their hypothesized punctuated events are the consequence of the sudden elimination of lineages, which then allows new taxa to invade and evolve in the now empty niches (see also Mayr, 1942; Gould, 1985). However, in contrast to animals, the plant fossil record does not show evidence of mass extinction (Willis and McElwain, 2002). The absence of plant mass extinctions has been attributed to the organisms' ability to withstand several environmental stresses (Grillo and Leone, 1995), to polyploidy [which also supports the notion that plants can evolve without the requirement of geographic barrier (Niklas, 1997)], hybridity (Rieseberg, 1995), asexual and mosaic reproduction (Niklas, 1997), and to the persistence of propagules (Shen-Miller et al., 1995), which is associated with the maintenance of cell membrane fluidity (Hardwood and Russell, 1984; Shen-Miller et al., 1995). Since the plant fossil record does not also include episodes of mass extinction, the idea that evolution proceeds in some way via the filling of empty niches (e.g., Mayr, 1942; Eldredge and Gould, 1972; Gould, 1985) fails as a general explanatory mechanism.

In presenting the "pulse model," which described apparently correlated organismal (specifically Pliocene-Pleistocene bovid) and environmental (wetter-drier) change, Vrba (1988, 1995) did not discuss mechanism. Nevertheless, the selectionist aspect of her model implies that multiple individuals experience identical molecular and morphological modifications as they track changes in their environment. Eldredge (2003) elaborated on Vrba's model by assuming that "already-generated genetically based adaptive variation" is conserved and available for organisms' use in new environmental conditions. He avoided the "hopeful monster" dilemma by arguing that widespread change in the



physical environment would impact most members of a species equally. But there is no evidence of a molecular system that “builds” organisms to be “adapted” to unforeseen physical and biological environmental changes. Even if true, though, Eldredge’s model of stasis conflicts with an assumption of conserved “genetically based adaptive variation.”

Our model incorporates information from a diversity of disciplines and does not sidestep the issue of multiple individuals inheriting the basis of sudden phenotypic change. We also identify an additional level (MPS) between the environment and the mechanism of gene expression and emphasize that the MPS is affected by changes in the environment (Fig. 3A).

In general, a given value of MPS derives from the integration of a finely tuned regulation of lipid metabolism and the assembly of lipids in cell membranes—processes that result from genetic changes occurring over geologically long periods of time and as physical environmental conditions gradually change. Organisms can adapt to their environment as long as MPS can adjust to varying conditions. When environmental change is rapid, cells cannot respond rapidly enough to compensate and adjust the lipid composition of their membranes, because this would require extensive modification of the transcriptional regulation of several genes and of the activity of their protein products (e.g., desaturases, elongases, phospholipases, flippases, and other enzymatic activities) responsible for assembly of phospholipids in the membrane.

### A THEORY OF SUDDEN ORIGINS

It is important to point out that HS genes represent a special class of genes whose products have multiple functions, including proper protein folding. Improperly folded proteins significantly affect key proteins responsible for genetic mechanisms, thus resulting in a stochastic increase in point and macromutation and thus an increase in the effective mutation rate. When a genetic change occurs in the recessive state, it will be passed on to subsequent generations and eventually be expressed “suddenly” in a homozygous condition in some number

of individuals. If these changes do not interfere with the organism’s ability to survive, the novelty may persist and spread across generations.

The “sudden origin” of genetic and phenotypic novelty results in “evolution.” We will not discuss whether “novelty” equates with “species,” but summarize consequences of this model, which, on a more theoretical level, was initially proposed by Schwartz (1999a, 1999b). First, one need not invoke a new model of inheritance to accommodate regulatory changes. Second, while complex molecular rearrangements, as well as the appearance of phenotypic novelty, are instantaneous events, the spread of the mutation(s) over some number of generations is (relatively) gradual. Third, the spread of the mutation(s) via heterozygosis will lead to the appearance of the phenotypic novelty in more than one individual. Fourth, these individuals will increase in number as heterozygotes continue to produce homozygotes, and as homozygotes breed with each other. Fifth, this model does not require scenarios of reproductive and/or geographic isolation for the emergence of novelty. Finally, there is no adaptive correlation between phenotypic novelty and the environment in which organisms with the novelty live; novelties persist if they do not interfere with their bearers’ viability or ability to reproduce. Interestingly, the facts of a “sudden origins” model—not just phenotypically, but genetically, and on structural as well as regulatory gene “levels”—were available before Morgan (1916, 1925) melded Mendelism and Darwinism into the model of population genetics that informed the evolutionary synthesis (Schwartz, 1999a).

If an organism’s features are not adaptations to specific environmental circumstances, we can decouple “evolution” and “adaptation.” The apparent “order” with which organisms seem to be distributed in nature results from the elimination of the “wrong” phenotypes, not necessarily the selection of better adapted ones. Phenotypes do not change to “fit” their environment as a result of “correct” sequences of mutation. Rather, the environment provokes organismal (plant and animal) change via stress.

Since the cause of cell function disruption is random, the resultant mutation’s effects on the regulation of development and its ultimate phenotypic expression are also random. In short, if a newly emergent phenotypic property does not kill you, you have it (Schwartz, 1999a).

Rutherford and Lindquist (1998) and Queitsch et al. (2002) proposed a neo-Darwinian mechanism that is regulated in *Drosophila* by the Hsp90 gene, but did not associate the emergence of new mutations with HSPs or the role of HSPs during gametogenesis. According to Rutherford (2003: p. 264), “chaperones do not alter the genotype, but rather the expression of genetic variations as phenotypic variations.” Rutherford and Lindquist (1998: p. 341) assumed that mutations in Hsp90 provide a “molecular mechanism that assists the process of evolutionary change,” but, as Dickinson and Seger (1999: p. 30) commented, “such interpretations seem to call for evolution of properties that anticipate future needs.” Further, while these studies on Hsp90 rely on the presence of variation, the underlying model does not address the emergence of variation.

The general picture of stability of organismal form in the fossil record suggests that morphology is linked to individuals’ environmental tolerance, which allows them to adapt, but not to evolve. The tendency “not to evolve” is probably due to what we could call DNA homeostasis, which is mediated, among other things, by adequate DNA-repair mechanisms. Significant deviation from a certain genomic arrangement likely causes either a reduction of homeostasis (fitness) and eventual death or, in some individuals, an opportunity for major DNA rearrangements, of which most will be lethal, but some compatible with life (Fig. 4).

No mechanism favors evolution. Biochemical and genetic conditions that could permit major genetic and sudden morphological novelty are very restricted, and the extent of morphological novelty is related to contingencies at different levels, from the homeostatic to the embryological, to protein structure, regulatory networks, and new environmental conditions. The collapse of homeostasis generates in a few individuals, and over a relatively short period of

time (a few generations), major, potentially nonlethal (therefore, “useful?”), rearrangements. The lack of something (homeostasis), rather than a persistent mechanism (constant mutation rate or natural selection), permits “evolution,” which may operate within a narrow range between the survival of the individual and its death through a completely chaotic mechanism that results from the lack of sufficient HSPs as a result of a genetically restricted MPS.

Our “sudden origins” model is compatible with current understanding of cell regulation and developmental genetics [and not necessarily incompatible with epigenetic models (Müller and Newman, 2003) given a broad concept of “mutation”], and we hope it will be tested by others, especially since a major implication is that current rates of environmental change, globally and locally, will lead to extinction, not to adaptation or evolution.

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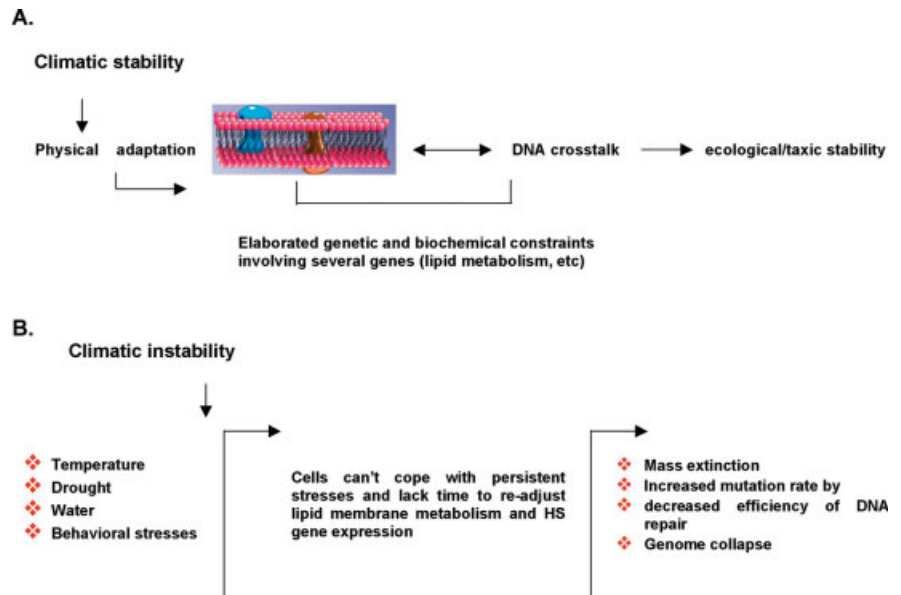
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**Figure 4.** Schematic representation of adaptation under stable climatic conditions (A) and effects of climate instability (B). The illustration is of a cell membrane. (Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com)).

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