Philosophica 58 (1996, 2) pp. 51-72

GOLDSCHMIDT'S HERESY AND THE EXPLANATORY PROMISE OF ONTOGENETIC EVOLUTIONARY THEORY

Scott A. Kleiner

ABSTRACT

Richard Goldschmidt has been cited for heretical views about evolution, particularly for his commitment to macromutation as an important component of evolution. He held views about genetic expression common among embryologists but rarely taken seriously by Anglo-American evolutionists. Weaknesses he saw in the explanatory power of neo-Darwinism are examined as well as the explanatory power of ontogenetic processes for evolution. This potential is now being realized in recent work in comparative molecular developmental genetics.

1. *Introduction*

Richard Goldschmidt enjoyed prominence as an evolutionary geneticist in Europe in the 1920's but had to flee Nazism in the 1930's. He was able to continue as a successful geneticist in the United States before his death in 1958. However his career in the United States coincided with a 'hardening' of the 'neo-Darwinian synthesis' wherein the principal objects of attention became gene frequencies in populations and the forces, particularly selection, that change or sustain them. Thus he became a popular target of criticism and even ridicule by defenders and practitioners of the Neo-Darwinian synthesis in its later stages of development (Gould, 1983).

Interestingly many of Goldschmidt's seemingly heretical beliefs have been borne out by recent efforts to incorporate ontogeny into the study of evolution (Gould, 1982). He was prone to statements that seemed absurd to many Mendelians, particularly his denial of the existence of the

particulate gene and his commitment to saltational evolution. In retrospect after molecular biology has given substance to some of the ontogenetic mechanisms he and other embryologists postulated, it has become clear that he was able to identify a number of explanatory deficiencies in neo-Darwinian practice and corresponding advantages to including ontogenetic mechanisms in evolutionary explanations. These deficiencies constitute problems whose importance is highlighted by a recognition of the explanatory promise of the ontogenetic approach. The assumption that ontogeny is a mechanism of evolution belongs to a tradition that originated in Germany in the 19th century but was eclipsed in Britain and the United States as embryologists turned from comparative to experimental embryology and evolutionary theorists embraced Mendelian genetics, which focused on transmission rather than development (Hambeurger, 1980). In continental Europe evolutionists continued to consider ontogenetic mechanisms worthy of study as an important component of evolution (Burian, et. al, 1988). However, these mechanisms are sometimes mentioned but never seriously considered by those committed to neo-Darwinism.

The aim of this paper is to explore some of the problems that continue to face the Neo-Darwinian tradition and to show that Goldschmidt's seemingly outlandish positions are actually a reasonable response to these problems at the time of his writing (1940). I shall elaborate and appraise the reasons Goldschmidt sets forth for believing that ontogeny has great explanatory potential. Finally I shall demonstrate how this promise is being realized in recent progress in comparative molecular developmental genetics. These points show that there is occurring a significant shift in the importance attached to various mechanisms of evolution: developmental epigenetic mechanisms will replace selection as the principal means by which evolving organisms are crafted. This position is one step beyond the recognition that neo-Darwinian adaptationism is inadequate because of 'developmental constraints' (Gould and Lewontin, 1978). According to the latter position selection is the principal creative force in evolution, but it is restrained by developmental organization which is necessary for the viability of the organism. According to the ontogenetic program, shifts in the epigenetic structure of development are the origin of phenotypic novelty in organically complex systems. This kind of developmental process is necessary though not sufficient (as a Lamarckian would claim) for the production of the kind of variation needed to generate the adapted-

ness and diversity that evolutionists seek to explain. Selection serves as a filter preserving only the more fit of these creations thereby assuring the adaptation of the preserved variant. Selection is by no means excluded from the evolutionary process, but its role is reduced from one of forming the complex organism to one of disposing the less fit products of the developmental process. The transition from neo-Darwinian to ontogenetic practice is a clear case of a revolutionary transition, since it is a replacement of core beliefs about mechanisms of evolution and their products and beliefs about their relative importance. A clarification of the reasoning behind this transition should be an important contribution to the logic of discovery.

2. *Goldschmidt's Heresy.*

In *The Material Basis of Evolution* (1940) Goldschmidt offers the following as 'basic assumptions':

> (a) Macroevolution cannot be conceived of on the basis of an accumulation of micromutations [as in neo-Darwinian practice]. ... (b) Macroevolution is accompanied by repatterning of the chromosomes [and thus a change in the inherited developmental system of the species] ... (c) An intrachromosomal pattern change may exert a considerable phenotypic effect independent of genetic changes [a process known as epigenetic amplification]. ... (d) Such a thing exists as a complete change of the reaction system based on a genetic change different from an accumulation of micromutants. We called such a change systematic mutation. (e) It is possible to produce immense phenotypic changes of a macroevolutional order by relatively small systematic mutations not involving the creation of anything new within the germ plasm. (f) The classical atomistic theory of the gene is not indispensable, for genetics as well as evolution. It is this theory which blocks progress in evolutionary thought.... We have already foreshadowed the twilight of the gene. (g) Models are available which make it possible to visualize the systemic effect of pure pattern changes in the germ plasm. (Goldschmidt, 1940, pp. 209f)

The first of these assumptions, (a), is a consequence of the others, particularly the distinction between *systematic mutations*, which are changes

in relational structures linking genes in the physiological processes causing their phenotypic expression, and *genic mutations*, or mutation in the genes themselves such as the generation of alleles. Macroevolutionary events, principally speciation events, are consequences of structural mutations and microevolutionary events, those changes within species that can be observed over the short term, are produced by genic mutations, according to Goldschmidt. Neither event excludes the occurrence of selection, which eliminates the products of both from a population or facilitates their spread through a population.

In defense of (a) Goldschmidt argues that there is an 'unbridgeable gap' between species which is qualitatively different from whatever separates populations that form subspecies, varieties or races. The Darwinian tradition has always assumed that the formation of races, varieties, subspecies, species, etc. are a continuous process without qualitative differences or differences in their causes.

According to Goldschmidt what prevents successful hybridization in sexual organisms occurs at the chromosomal level. Comparison of the chromosomes of the closely related species *Drosophila pseudoobscura* and *Drosophila miranda* shows rearrangement of chromosomal material that exemplify his systematic mutations. He assumes here that the action of a gene can be greatly influenced by its location on a chromosome relative to other genes, the 'position effect'. Neo-Darwinians downplay the importance of this effect, but for Goldschmidt these mutations reorder the developmental systems acting in the ontogeny of individuals. What keeps species genetically distinct is an incompatibility of their two developmental systems so that when they are combined together in the hybrid the development of a viable or fertile organism is physiologically impossible. Because of the position effect systematic mutations that isolate new species can be expected to also produce significant phenotypic changes. Though Goldschmidt could not have known this in 1940, these implications of systematic mutations anticipate 'punctuated equilibrium' proposed by paleontologists (Gould and Eldredge, 1977, Stanley, 1979), according to which the major phenotypic changes occur at times of speciation, not during angenic evolution, that is evolution in lineages that do not split.

It might seem that Goldschmidt's view of speciation is not entirely borne out by recent studies, many of which suggest that geographical, behavioral, and ecological isolation are the most important factors in

initiating and maintaining genetic isolation between populations. However geographical isolation is not genetic, and none of these isolating mechanisms exclude Goldschmidt's karotypic incompatibility as a means of accounting for hybrid inviability or infertility. Also most recognized species differ in chromosomal number and configuration, which confirms Goldschmidt's point. Furthermore the genetics of isolating behavioral differences is not completely known, so at present there is nothing to exclude their being products of Goldschmidt's systematic mutations.

Goldschmidt also holds that timing of developmental episodes, such as the growth of various body components or the onset of sexual maturity, is genetically determined and subject to significant shifts as a consequence of small systematic mutations. A systematic or genic mutation can alter this timing rendering the relative timing of an episode earlier or later in the developmental process. This mechanism, called heterochrony, can render a character vestigial or eliminate it entirely by delaying its development. Another process, called allometry, may also have large phenotypic effects by altering the relative rate of growth of various bodily components.

These evolutionary mechanisms can be inferred from embryonic recapitulation, a thesis put forth in the nineteenth century by Karl Ernst von Baer. Goldschmidt gives the following illustration of recapitulation:

> If macroevolutionary changes proceed by mutations affecting the rate of embryogenetic processes at a definite time in development, the ontogeny of all descendants of the mutant form must continue along ancestral lines up to the stage in development first affected by the mutant. Obviously, the mechanics of development do not permit any other course. If the mutation which changed the long tail of Archeopteryx, with its segmental tail feathers, into the rudimentary tail of birds with fanlike tail feathers, occurred in such a way that after formation the tail segments were made to grow together, etc., the present embryology of birds must necessarily contain an Archeopteryx stage, which is actually the case.... If the mutation in question had changed tail segmentation primarily; i.e., before the stage of visible segmentation, no recapitulation of the Archeopteryx condition would occur in the embryogeny of birds. The presence of recapitulation shows positively that the original mutational change in the ancestors affected development after the stage which is recapitulated. The fact that recapitulation is an ubiquitous feature of development suggests that macroevolution

> has progressed mainly by this type of change. The reason is obviously to be found in the relation between the genetic basis and the physiology of development: a genetic change affecting the rate, time of inception, time of determination, range of regulatory ability of embryonic processes, may occur in a single step without requiring a rebuilding of much of the genetic material. The genetic change is probably a permutation of some of the genetic elements controlling development, whatever theory of such changes we choose to accept in detail, and does not require the origination of new genetic determiners or determining systems. (1940, p. 390)

Recapitulation allows an inference from embryonic processes to mechanisms for ancestral evolutionary events which replaces the Neo-Darwinian inference from micro- to macroevolutionary mechanisms. For example, the recapitulation of the *archeopteryx* tail in embryonic birds allows one to infer that a mutational event distinguishing descendant birds from the ancestral *archeopteryx* had the macromorphological effect of fusing of the vertebral segments. What caused this evolutionary event is the mechanism to be found in what causes the fusion of embryonic vertebral segments. One can also infer polarity in evolution from embryonic processes, viz. that the ancestral traits are what appear first, the long segmented tail, and derived traits appear later in development, the fusion of the tail segments.

Thus the uniformitarian methods of neo-Darwinism cannot be defended as the only means by which evolutionary mechanisms can be inferred. Also exceptions to von Baer's principle may occur if the development of adult stages is accelerated so that they appear in juveniles or if the juveniles take on particular adaptations to the conditions they face, e.g. adaptations for dispersal or concealment from predators (DeBeer, 1951). Hence recapitulation remains a fallible procedure for inferring ancestral characters.

In addition to recapitulation, Goldschmidt subscribes to another thesis attributed to von Baer: This is the thesis that the earlier stages of development are more fundamental in the vital functioning of the organism and are thus least likely to change. Thus he tells us:

> ... a genetic change involving a huge qualitative departure which would completely revolutionize the processes of development from their very initiation, would wipe out the possibility of recapitulation and would mean such an immense departure that it probably could rarely if ever

> lead to a viable product. A viable product would be a new phylum. (1940, p. 390)

The cascading of epigenetic processes means that early mutations will change the whole course of subsequent development, where the later events depend on the occurrence of the earlier. Though effects of mutations acting earlier are epigenetically magnified, they are more likely to be deleterious than mutations having effects on later events with fewer subsequent consequences. The later stages are less fundamental and can change with less likelihood of disrupting vital functions in an organism. Thus mutations acting late in development are the most likely to be retained in a lineage, and therefore there should be more of them as in the increasing branching of the phylogenetic tree.

It should be noted that this argument presupposes the occurrence of natural selection. Without natural selection all mutations affecting development would be equally likely to be retained. Hence Goldschmidt's ontogenetic theory must supplement natural selection and cannot be construed as replacing or excluding it. Also these points don't rule out the possibility of a successful mutation in early stage regulation, which can account for differences between higher taxa, such as classes or phyla. In more primitive organisms the selectional constraints against this kind of mutation could be less, as there is less downstream function to disrupt (Goldschmidt, 1940, p. 269). An example of something like this process in the formation of new phyla will be discussed below.

3. *The Mendelian Gene and Neo-Darwinism*

During much of Goldschmidt's career there was little beyond speculation regarding what the Mendelian gene was. Thus Dobzhansky tells us:

> The sole evidence of the occurrence of a change in the gene is the appearance of a phenotypic variant, a mutant, which follows Mendel's law of inheritance. Yet a loss (deficiency) or a reduplication of a part of a chromosome likewise results in phenotypic alterations that show Mendelian inheritance. Similar effects may be produced by rearrangements of the genetic materials within the chromosomes (inversion, translocation). Finally, reduplications and losses of whole chromosomes may simulate Mendelian units. (1951, p.27)

Without theoretical descriptions identifying genes as specifically bounded segments of DNA and molecular methods for identifying specific genes, reference to genes must be channelled through phenotypic manifestations that display significant heritability. That is, if one presumes a one to one relation between genotype and phenotype, heritable phenotypic differences will serve as markers for genotypic differences, and under this presumption heritable phenotypes will identify allelic differences by either description in theoretical discourse or possibly ostention in an experimental context. However the one-one linkage between phenotype and genotype is incoherent with other Mendelian conceptions such as those of recessiveness, pleiotropy and multigenic quantitative characters. The only instances in which such a relation is clear and reliable are the biochemical 'phenotypes' revealed in the 1960's by electrophoretic and immunological experimental methods. No thoughtful Mendelian in the first half of this century would actually believe that such a relation exists, but they did often speak as if phenotypic and genotypic variation are exactly correlated. This point is in evidence in two distinct ways of describing Sewall Wright's 'selective landscapes'. One is Wright's own "...the species is thought of as located in gene frequency space. ...Evolution consists of movement in this space." (Wright, 1969, p. 472; quoted in Michod, 1981, p. 3) By contrast, G.G. Simpson speaks of grazing and browsing 'peaks' in the landscape, where grazing and browsing are behaviours and must be considered phenotypic (Simpson 1953, p. 157; quoted from Grene 1958, pp. 118f). That this ambiguity has not been attended to is evidence of the easy but unthinking transition from discourse referring to heritable phenotypes to that referring to genotypes.

Procedures have been developed in Mendelian practice for rendering reference to genes more definite: Recessives can be identified by inbreeding so that the homozygous recessive can be marked, e.g. as the character occurring in about one quarter of the progeny thus produced. However, this procedure is not completely reliable because it presumes linkage can be ignored and that the progeny thus produced are equally viable. Complementation tests can show whether alleles occur at the same or different loci. However, this test can fail if modifier genes are involved in the recombination that is supposed to restore wild type phenotypes for both presumed loci. Also T.H. Morgan estimated the locations of genes on *Drosophila* chromosomes by determining their linkage with known observable markers, both anatomical markers such as bands on the chromo-

some and genetic markers whose location is already known. The assumption behind this method is that the closer two genes are on a chromosome the more likely it is that they are inherited together. Again there are significant exceptions because rates of recombination can vary with different locations among chromosomes. Also the same anatomical markers on the chromosome can also show whether Mendelian phenotypes are produced by changes in the organization of the chromosome such as inversions and translocations. As Goldschmidt claims, such happenings need not be accompanied by changes in single genes, allelic changes.

As long is it remains possible that the phenotypic markers are produced by varying numbers of genes or by karyotypic variation, these methods for determining genotype-phenotype associations are far from giving a complete and reliable account of the genetic basis of Mendelian phenotypic characters. Though they may provide means of referring to genes by proxy, where reference is accomplished by descriptions in a context in which one can differentiate and localize the object of reference, the differentiation and localization fall short of what at the time was a conceivable and desirable identification of the gene. For many demonstrably heritable character differences the question 'What causes these differences?' remained open, having as possible answers chromosomal as well as genic alleles. Also the question 'What is the gene?' remained open. Genes had not been placed in the compositional hierarchy emerging from cell theory and biochemistry at the turn of the century. Though they could be located on chromosomes, it was yet to be determined whether they are morphological structures or chemical substances. One constraint on this last question was that an acceptable answer provide an account the seemingly vast variety of information that genes carry, viz. genetic specificity, and of the replication of genetic specificity, which is central to Mendelian inheritance.

To one with a background in developmental biology such as Goldschmidt, the one to one relation between genotype and phenotype presumed in much of Mendelian practice is incompatible with the epigenetic structure which embryologists at the time believed to underlie the heritable programs of ontogenesis. Thus from Goldschmidt's vantage point, Mendelian genetics and the neo-Darwinian program, which incorporates Mendelian principles into its conception of evolution as changing gene frequencies in populations, suffer from both internal and external coherence problems. These problems make reference to individual or discrete

genes at best indefinite and uncertain, leaving much room to doubt the actuality of atomistically acting genes. Larry Laudan has cited such coherence problems as among the types of weakness that lead to the abandonment of a research tradition if a rival tradition can solve them (Laudan, 1977). Goldschmidt's doubts thus can be construed as reasonable on grounds of Laudan's account of how problems are highlighted. A problem facing one tradition is enhanced in importance if another tradition holds promise for its solution.

Goldschmidt thus views embryological epigenetics as incompatible with a constitutive assumption neo-Darwinian practice, viz. that the organism can be broken down into an aggregate of Mendelian unit characters and their variants. Neo-Darwinism seeks the explanation of the occurrence of these characters, or their relative frequencies in a population by finding causes that determine the change of frequency of each character separately. This procedure constitutes a 'positive heuristic' (Lakatos, 1970, Michod, 1981) in neo-Darwinian practice for solving problems of explaining evolutionary processes, where these processes are held to be trajectories of gene (allelic), genotype, or heritable phenotype frequencies in a population. This heuristic, 'beanbag genetics' uses Hardy-Weinberg equilibrium as a null hypothesis, and considers selection, mutation, migration, drift and assortive mating as possible forces that move a population state from equilibrium frequencies. Beanbag genetics has an advantage of allowing relatively simple calculations of genic trajectories. The 'gene's eye view' popularized by Dawkins, whereby one looks for strategies by which a gene can enhance its representation in subsequent generations, can be considered further articulation of beanbag genetics. Some have contended that this procedure can be justified theoretically if one presumes a constant genetic background for the variant alleles (Sterelny and Kitcher, 1988), but given the considerations Dobzhansky sets forth in the above quotation, such presumptions are patently unrealistic and the only justification that can be given for beanbag genetics is its heuristic merit. The 'Darwinian' portion of beanbag genetics views selection as the principal force driving evolution, and accordingly another heuristic assumption is that each allele at a given locus makes an additive contribution to the fitness of the organism in question (Williams, 1966).

Single locus models also ignore the linkage between genes as they are strung on a chromosome. Linkage implies that alleles that are located on

a single chromosome are more likely to be inherited together the closer they are to one another. Linkage disequilibrium models take into consideration the effects of linkage, but supporting arguments for the beanbag heuristic show that linkage diminishes in importance for relatively high rates of recombination and low values for selection differences (Clegg, 1978, from Michod, 1981, 14n). This result illustrates Lakatos' positive heuristic of turning *prima facie* anomalies into successes. One further ramification of this positive heuristic is the belief that the best prospect for progress is not by considering more interacting loci, but by further inquiring into the forces acting on a given locus (Michod, 1981, p. 14).

Lakatosian methodology also prescribes that these heuristics be maintained as long as the program is 'progressive', that is as long as it generates a succession of models with ever increasing power of anticipating novel fact. 'Novel fact' might best be interpreted rather broadly to include predictions in conflict with received belief and unexpected predictions in the sense that there was no belief on the matter regarding which the model provides information. In the 1920's, 30's and 40's beanbag genetics has had rather remarkable success on these counts. Some of the more influential victories are as follows:

(i) Single locus models demonstrated that under very weak selection relatively few generations are required to drive a population to the fixation of the favoured allele, as shown by Norton, Haldane and Chetverikov on various occasions between 1915 and 1924 (Michod, 1981, pp. 16f). Many opponents of selection from the time of the earliest reviews of Darwin's *Origin* expected that selection could not maintain the rare adaptive variants, which would be lost by blending back into the parent population (Hull, 1973, Provine, 1971). Mendelian genetics disallowed blending but at the same time seemed to favour non-Darwinian saltational evolution. This result and (ii) Fisher's account in 1918 of quantitative variation in terms of multiple independent Mendelian loci eliminated these seeming incompatibilities between Darwinism and Mendelism. This achievement of coherence between Mendelism and Darwinism is perhaps the most important step in the development and widespread acceptance of neo-Darwinism among biologists in the 1930's.

(iii) In 1924 Haldane showed that the same kind of model predicted the unexpected result that deleterious, even lethal genes, can be 'carried' for many generations if their heterozygotes were viable. This outcome

was contrary to the beliefs of many, including advocates of eugenics, who thought that selective breeding could completely remove deleterious genes from a population.

(iv) In cases of partial dominance, viz. where the heterozygote is intermediate in fitness between the two homozygotes, selection of more fit alleles favours homozygosity, as does genetic drift in which genes can become fixed by a random walk in a finite population (Lewontin, 1974). Selection acting on genotypes that are polarized into homozygotes will eliminate all but one allele. The additive effects of this process over all loci in a population generate a monomorphic population, a population in which there is no genetic variation and in which further evolution could not occur. This consequence is the 'classical hypothesis' that most genetic loci are homozygous for wild type genes as preserved by selection. Within the framework of the beanbag program the classical hypothesis implies that the variation necessary to feed selection must be produced by mutations because the atomization of Mendelian characters rules out mutants from chromosomal changes. This is a source of empirical problems for the classical hypothesis and the beanbag models that seem to support it because the frequencies of mutations, *a fortiori* favourable mutations, is too low to sustain evolution at a plausible rate.

An attempt to resolve this problem was to introduce the balance hypothesis, according to which latent polymorphism in a population provides ready-made the variation needed to feed selection. This step is a shift in the 'core' assumptions of neo-Darwinian evolutionary research about its subject, populations, and it significantly revises the conception of species from the monomorphic classes of the essentialists to polymorphic historical 'individuals' (Hull, 1978). The balance hypothesis is supported by empirical evidence of biochemical alleles and by models (v) originally put forth by Fisher in 1922 in which heterozygote superiority can sustain polymorphism in a population. These models are another seeming success for beanbag genetics. Beanbag genetics may have anticipated the possibility of stable polymorphisms, though it could provide no grounds for anticipating high levels of polymorphism in a population because according to the heuristic assumption of independence between loci, heterosis at one locus provides no reason for believing that heterosis exists at another, much less many loci. There are also serious problems concerning the genetic load implicit in efforts to explain widespread heterozygosity by heterosis, and some have resorted to the assumption

that polymorphism is due to selectively neutral alleles. The 'neutral theory' is a departure from neo-Darwinian adaptationism, the belief that every character is an adaptation, that is, its presence is due to selection.

In sum, beanbag genetics has had significant success, and its positive heuristic is still considered to be promising. The problem of providing a selectionist account of stable polymorphism remains unsolved, though some new positive sub-heuristics are being tried, such as considering time and space-dependent selective forces. Another approach is to use linkage models (Spencer and Marks, 1993), but this is a departure from beanbag genetics or a revision of its negative heuristic according to which genic and phenotypic atomism should be retained.

4. *Molecular developmental genetics.*

Given the problems concerning the indefiniteness and unreliability of pre-molecular references to genes and the coherence problems facing the beanbag program, Goldschmidt's claims concerning the demise of the Mendelian gene should not seem completely absurd at the time he made them. As a developmental geneticist Goldschmidt had good reason to reject the implicit one to one correspondence between genotype and phenotype and the atomization of both the genome and the organism as incompatible with the epigenetic network of genes believed to cause phenotypic traits. Molecular methods of localizing, sequencing and comparing gene sequences have given much of the sought after referential specificity to the gene concept and Goldschmidt's rejection of the gene as a unit of mutation is no longer credible. The same developments have also given more specific substance to other concepts in Goldschmidt's thought, particularly the genetic relational structures that he believed were responsible for speciation and development.

Methods for sequencing genes (Culp, 1995) produced knowledge of conserved segments that have been identified as 'promoters' and 'stop codons' which can be used to identify the boundaries of an individual gene on a strand of DNA. It is thus that genes have been located in the hierarchical compositional scheme as macromolecules of DNA appearing in both nuclear chromosomes and in cytoplasmic organelles such as mitochondria. The power to identify specific genes within and across species has become part of the practice of genetics. A gene (type) can be

identified by its sequence and the same gene (type) can be replicated many times over (many tokens can be produced) by cloning or *in vitro* polymerase reactions. Importantly for ontogenetic evolutionary theories it is possible to identify genes that occur in different taxa.

Ontogenetic theory now incorporates the following beliefs and concepts which provide more details about presumed components of developmental systems than could have been possible for Goldschmidt: Metazoan development consists in the differentiation of cell types, cell migration, adhesion, growth and death, all of which are mechanisms of morphogenesis. These processes are controlled by genes whose expression is regulated by the products of other genes, usually proteins. Regulation takes place at the several stages of gene expression described by the central dogma, at transcription (DNA → RNA) and translation (RNA → protein) and post translationally. Models of gene regulation originated from studies of bacterial characteristics such as those of Jacob and Monod in 1961, and Engleberg in 1965 concerning the production of substances for bacterial metabolism. The original models include negative and positive regulation of the production of messenger RNA (mRNA), which is regulation at the first stage of gene expression. This regulatory model has been extended to eukaryotic cells, the cellular components of metazoans, with some additions and complications. These include tissue specific regulatory sites within the genes, enhancers and repressors, and the regulatory roles of the various membranes between and within cells, where regulation can be effected by various means of controlling the distribution of transcription factors. Also various proteins, such as histones, which bind and configure the DNA in the eukaryotic chromosomes, can contribute to the regulatory process, and may be the mechanism by which cells become determined or specialized in ontogeny. Other possible regulatory sites include posttranscriptional occurrences, e.g. regulatory substances can control the duration of RNA and can form various modifying complexes with other proteins in the regulatory process. In the case of metazoans, these regulatory proteins can be produced maternally, e.g. in the maternal tissues surrounding the developing egg, as well as at various sites in the developing embryo.

Regulatory mechanisms are assembled into a complex of interlocking networks and loops making possible cascades of stimulation and inhibition and feedback control (Kauffman, 1986). Also fields or gradients of morphogens and the timing and process of their distribution in a region,

require the consideration of inter- as well as intracellular structures as part of the ontogenetic system. Gradients of transcription factors on various axes of the embryo, e.g. anterior-posterior, dorsal-ventral, or proximal-distal in the case of appendages, act as stimulators and repressors in the production of heads, tails, segments, digits, etc.

A good deal of molecular developmental genetics has focused on just a few model organisms that are well known to geneticists, viz. the fruit fly *Drosophila Melanogaster*, the nematode worm *Caenorhabditis elegans*, and the mouse *Mus musculus*. However, an interest in the evolutionary import of developmental structures requires comparative studies of the developmental genetics of a wider range of organisms (Raff, 1992). If we apply the principle of parsimony (described in section 2) to ontogeny we would expect considerable homology among the developmental systems of metazoic organisms separated by taxonomic differences at all levels, particularly in the fundamental mechanisms of cell differentiation in the early stages of development. Also the organization of ontogenetic structures into cascading events of stimulation, inhibition and feedback implies Von Baer's principle and all of its evolutionary consequences, particularly an increase in the frequency of successful mutations as they affect later stages of development. Accordingly we would expect a homologue of von Baer's law to hold at the molecular level: Metazoans share developmental mechanisms that are active in early developmental stages but these mechanisms diverge with the taxa in later stages. Furthermore any modifications of the early stages that are viable will have, by virtue of their influence on subsequent cascading developmental events, magnified effects on the phenotype. These effects correspond to Goldschmidt's speculations about macromutations, and their possibility is clearly envisaged in this scheme for developmental systems. Macromutations are a product of 'epigenetic amplification' which need not occur at early embryonic stages. Regulatory mutations acting at later developmental stages can amplify because of their effects on differential rates of growth or on the timing of developmental events.

Some of Goldschmidt's conjectures have been borne out in the discovery of the 'homeobox', a widely conserved protein sequence of 60 amino acids that binds DNA and regulates the expression of genes such as the HOM family. The HOM genes specify regions of cell determination (fields) along an axis (anterior-posterior or dorsal-ventral) in an embryo. The cDNA derived from this regulatory protein hybridizes with

a number of other genes known to play a role in development, e.g. *antennapedia* (a gene regulating the production of legs and antennae), *ftz* (*fushi tarazu*, a gene that plays a role in defining parasegment boundaries) and *Ubx* (*Ultrabithorax*) another gene involved in axial specification. Once this protein is identified in one organism, reverse transcription is used to generate a segment of c-DNA for *in situ* hybridization experiments in order to locate for cloning and sequencing other regulatory genes in the same or in different taxa. It is thus that specific regulatory genes can be identified and can be compared for similarity within and between taxa. Similar sequences can be and have been found in the genes of other organisms as widely separated taxonomically as insects and vertebrates, which fall in distinct sections of the subkingdom Metazoa, Protostomia (including nematodes, annelids, mollusks, arthropods) and Deuterostomia (containing echinodermata, hemichordates and chordates). In each taxon there are groups of such regulatory genes, such as the HOM group, that bear one to one homologies with genes in other taxa. Also the order of these genes on the chromosome is conserved across these sections and there is a correlation between location on chromosome and location of the region of expression on the body axis of the embryo in both vertebrates and insects. For example there are segments in chick and the mouse hindbrains that are developmentally homologous to the parasegments of the fruit fly embryo in that both are regulated by homologous families of genes, the HOM family. So it is suggested that this developmental pattern is ancestral and preserved in both sections, but in the case of the vertebrate much else is added beyond what occurs in the hindbrain (Lawrence, 1992). These points articulate and confirm Goldschmidt's claim that the order of genes on the chromosome have developmental significance and von Baer's principle that phylogenetically earlier patterns are ontogenetically more foundational and are more widely conserved among the taxa.

Further developments of the ontogenetic approach include a recent proposal (Davidson, et. al. 1995) regarding the mechanism by which bilaterian body plans emerged from a common ancestor to the bilaterans and the radiata. (Bilaterans include two sections of the subkingdom Metazoa: the Protostomia, and Deuterostomia. Radiata is another section of this subkingdom, including hydra, jellyfish, sea anemones, and corals). Many bilaterans undergo type 1 embryogenesis in which the adult stage is preceded by a free swimming and feeding microscopic larva of a few

hundred or thousand cells and having no resemblance to the adult. This kind of metamorphosis is different from the kind often seen in insects and vertebrates, in which major features of each such as segmentation and the dorsal nervous system appear in both larvae and adults. Presumably this latter pattern of development evolved from the former as the period of the earliest embryonic stages were shortened and certain adult features appeared precociously. Both kinds of development are often found among marine organisms of the same genus, suggesting that the transition from type 1 to more direct forms of development occur commonly. Thus the mechanism for such transitions must be one whose occurrence is of relatively high probability.

The regulatory genetics in the development of type 1 larvae is quite different from that appearing in adult morphogenesis. Larval differentiation is regulated by products that are expressed in the first cleavage divisions, whereas in adult development further regulatory products differentiate within these initially specified lineages and are not limited to them in their distribution and subsequent action. In adults regional areas of differentiation and subdifferentiation are defined across cell lineages by gradients of morphogenic regulators that control specification, division, adhesion and movement among the cells. These begin with axial and circumferential differentiation, and these fields are further subdivided as development proceeds. In the type 1 embryo metamorphosis is a product of the adult pattern of development acting from set-aside cells in the larva, where the behaviour of these cells is relatively independent of the larval developmental program. This type of larva is supposed to provide the primitive platform upon which divergence into the macroscopic sections of radiata, protostomia and deuterostomia is founded, an event that presumably took place in the late precambrian era (Davidson, et. al. 1995, p. 132l). It is supposed that these set-aside cell groups were freed of the growth constraints applying to the larval cells much as the misexpression of oncogenes produce unregulated growth in mammalian cancers. The removal of these constraints are thus relatively probable occurrences, thereby making possible a number of independent evolutionary events leading to diverse taxa. Accordingly, developmental constraints can be reduced opening up the possibility of novelty and rapid differentiation among novel downstream developmental structures. Thus we have a plausible mechanism for the Cambrian explosion. An explanatory advantage of this mechanism is its relatively high probability as

compared to the low probability of large numbers of selectively advantageous allelic substitutions.

5. *Conclusions*

Although at the time of Goldschmidt's writing there is little explicit evidence for the postulated regulatory structures, their explanatory potential for both developmental genetics and for evolution is apparent: Recapitulation contributes to parsimony in evolution because the improbable events of the evolution of complex developmental systems need not occur repeatedly, which would entail geometrically decreasing probability for such compound events. Instead these events need occur only once, and the systems then are propagated by pervasive processes of inheritance through all of the metazoic phyla. It is difficult without considering development to determine how to atomize an organism into independently evolving characters because in many cases ancestral alleles have been removed and also because a single gene can regulate the production or the relative rates of growth of several features. Epigenetic amplification can explain the apparent rapidity of some of the evolutionary events believed to be in evidence in the fossil record. The need for many improbable favourable mutations in the gradual evolutionary process is an unsolved explanatory problem for the classical selectionist, particularly where the fossil record shows evidence of that evolution consists of stable periods punctuated by episodes of very rapid radiation of new species (Gould and Eldredge 1977, Stanley 1979, Lovtrup 1987). Also as long as balance selectionism has no satisfactory account for stable polymorphisms, rapid evolutionary episodes remain problematic.

According to standard abductivist methodologies (e.g. Hanson, 1961, Salmon, 1966) reasoning to an explanation provides grounds for *entertaining* a hypothesis for further research, though such argumentation should not be sufficient for its acceptance. This qualification is appropriate, for it would be mistaken for a scientist or philosopher to presume *a priori* that natural processes actually take the form that appears in a given intelligible pattern. Direct evidence, prior credibility, and consilient indirect evidence for the explanatory patterns are needed for their acceptance. Goldschmidt's case is primarily abductive, but it has the consequence that evolutionists should take seriously the explanatory potential

of epigenetics and recapitulation. They should entertain the possibility of macroevolutionary events, and accordingly should be cautious in their easy inferences from micro- to macroevolution. They should also attach importance to the conceptual and empirical problems of specifying epigenetic mechanisms as potential contributors to the explanatory success of evolutionary theory. The expected contributions will include a better explanation of punctuated evolution, better knowledge of phylogenetic relations, and the genetic explanation of phenotypic effects of regulatory mutation. Epigenetic models could predict heretofore unknown types of phenotypic mutation, including unsuspected macroevolutionary events in the past.

Several features of the ontogenetic program enhance its explanatory power: Knowledge of epigenetic mechanisms in a single organism should provide knowledge of the effects of different kinds of mutation, whether systematic (in regulatory genes or in chromosomal rearrangements) or other (the production of new alleles in structural or housekeeping genes, the activation of inactive pseudogenes). This potentiality should be considered in contrast to the neo-Darwinian 'mutation', which is essentially the production of new alleles in a completely undirected manner. Epigenetic variation should not, as sometimes occurs, be confused with Lamarckian 'directed' mutation where an organism can directly adapt itself to its environment and these adaptations can become heritable. Epigenetic variation is directed by the internal environment of the organism, particularly its developmental program. Though this program requires suitable external environmental conditions for its phenotypic expression, and may have the capability of directly adapting to some of these conditions, it may preserve but does not necessarily generate heritable adaptations.

Furthermore the mechanisms postulated by the ontogenetic approach are those which can be presumed relatively likely or relatively common. Neo-Darwinian theory has problems with compounding improbabilities: If the organism is atomized into multiple independently evolving Mendelian unit characters, the low mutation rate combined with the high probability that a mutation is deleterious is further compounded by the need for many favourable mutations. Epigenetic amplification, allometric growth and heterochrony are among the concepts of developmental genetics that can be combined in specific cases to enhance the probability of favourable mutations by reducing this compounding. By providing grounds for rendering evolution, particularly rapid phyletic diversifica-

tion, more probable, the ontogenetic approach has more explanatory power than present models in neo-Darwinian practice.

Finally, the beanbag program, which is an important positive heuristic for neo-Darwinism, though successful in generating unanticipated novel predictions, is faced with both conceptual and empirical problems whose solution is a plausible product of the ontogenetic approach: The single-locus models are admittedly unrealistic, and efforts to make them more realistic face many technical difficulties. The assumption that phenotypic alleles are Mendelian genotypes is incoherent with beliefs about the physiology of gene expression. These constitute internal and external conceptual problems for that particular heuristic which are highlighted in their importance in the ontogenetic program, though it can hardly be said that the latter program has solved these problems. Finally, the neo-Darwinian program has yet to solve the problem of stable polymorphic populations. Since this is a problem in population genetics, it is outside of the domain of epigenetic theory. However problems concerning stability and homeostasis are within that domain, and potential solutions to these can contribute to the articulation and explanatory power of neutralist and quasi-neutralist theories of polymorphism.

The ontogenetic approach to evolutionary theory has great potential for novel explanatory insight into the evolutionary process. This potential was fairly clearly seen by Goldschmidt and a number of others with knowledge of epigenetic processes, including DeBeer, Waddington, Needham and Lovturp. Some of this potential is now being realized in recent programs of comparative molecular developmental genetics. These are grounds for evolutionists to look beyond the domain of population genetics to developmental genetics as promising a deeper insight into evolutionary processes.

University of Georgia

REFERENCES

Burian R., Gayon J. and Zallen D. (1988), 'The Singular Fate of Genetics in the History of French Biology, 1900-1940', *Journal of the History of Biology* **21**, pp. 357-402.

Clegg M.T. (1978), 'Dynamics of Correlated Genetic Systems. II. Simulation Studies of Chromosomal Segments Under Natural Selection', *Theoretical Population Biology* **13**, pp. 1-23.

Culp S. (1995), 'Objectivity in Experimental Inquiry: Breaking Data-Technique Circles', *Philosophy of Science* **62**, pp. 438-458.

Davidson E.H., et. al. (1995), 'Origin of Bilaterian Body Plans: Evolution of Developmental Regulatory Mechanisms', *Science* **270**, pp. 1319-25.

DeBeer G.R. (1951), *Embryos and Ancestors*. Oxford UK: Clarendon Press.

Dobzhansky T (1951), *Genetics and the Origin of Species*. 3rd Edition, New York NY: Columbia University Press.

Goldschmidt R. (1940), *The Material Basis of Evolution*. New Haven CT: Yale University Press.

Gould S.J. and Eldredge, N. (1977), 'Punctuated Equilibria: The tempo and mode of evolution reconsidered', *Paleobiology* **3**, pp. 115-51.

Gould S.J. and Lewontin, R. (1978), 'The Spandrels of San Marco and the Panglossian Paradigm: A critique of the adaptationist programme', *Proceedings of the Royal Society* **205**, pp. 581-598.

Gould S.J. (1982), *The Uses of Heresy: An Introduction to Richard Goldschmidt's The Material Basis of Evolution*. New Haven CT: Yale University Press.

Gould S.J. (1983), 'The hardening of the modern synthesis', in Grene, M. (ed.), *Dimensions of Darwinism Cambridge*. UK: Cambridge University Press, pp. 71-93.

Grene M. (1958), 'Two Evolutionary Theories', *British Journal for the Philosophy of Science* **9**, pp. 110-127, 185-193.

Hanson N.R. (1961), *Patterns of Discovery*. Cambridge, Cambridge University Press.

Hambeurger Viktor (1980), 'Embryology and the Modern Synthesis in Evolutionary Theory', in Mayr, E. & Provine, W. (eds.) *The Evolutionary Synthesis*. Cambridge MA: Harvard University Press

Hull D. (1973), *Darwin and His Critics: The Reception of Darwin's Theory of Evolution by the Scientific Community*. Cambridge MA: Harvard University Press

Hull D. (1978), 'A Matter of Individuality', *Philosophy of Science* **45**, pp. 335-360.

Kauffman, S. (1986), *The Origin of Order*. Oxford UK: Oxford University Press.

Lakatos I. (1970), 'Falsification and the Methodology of Scientific Research Programmes', in Lakatos, I. and Musgrave, A. (eds.) *Criticism and the Growth of Knowledge*. Cambridge: Cambridge University Press.

Laudan L. (1977) *Progress and its Problems*. Berkeley CA: University of California Press

Lawrence P.A. (1992), *The Making of a Fly*. Oxford UK: Blackwell Scientific Publications.

Lewontin R. (1974), *The Genetic Basis of Evolutionary Change*. New York NY: Columbia University Press.

Lovtrup S. (1987), *Darwinism: The Refutation of a Myth*. New York NY: Croom Helm.

Michod R.E. (1981), 'Positive heuristics in evolutionary biology', *British Journal for the Philosophy of Science* **32**, pp. 1-36.

Provine W.V. (1971), *The Origin of Theoretical Population Genetics*. Chicago IL: University of Chicago Press.

Raff R.A. (1992), 'Evolution of developmental decisions and morphogenesis: the view from two camps', *Development* 1992 Supplement, pp. 15-22.

Salmon W. (1966), *The Foundations of Scientific Inference*. Pittsburgh, PA: University of Pittsburgh Press.

Simpson G. (1953) *The Major Features of Evolution*. New York NY: Columbia University Press.

Spencer H.G. and Marks, R.W. (1993), 'The evolutionary construction of molecular polymorphisms', *New Zealand Journal of Botany* **31**, pp. 249-256.

Stanley S.M. (1979), *Macroevolution: Pattern and Process*. San Francisco CA: Freeman.

Sterelny K. and Kitcher, P. (1988), 'The Return of the Gene', *Journal of Philosophy* **85**, pp. 339-361.

Williams G. (1966), *Adaptation and Natural Selection*. Princeton NJ: Princeton University Press

Wright S. (1969), *Evolution and the Genetics of Populations. Vol. II. The Theory of Gene Frequencies*. Chicago IL: University of Chicago Press.