Natural selection acts on variation, but how does that variation come into existence? The debate regarding creation of evolutionary novelties dates back to the early twentieth century, a time before substantial molecular data was acquired. This narrow approach, though, limited the vision of many scientists, most notably Simpson and Goldschmidt. Evolutionary novelty, however defined, has integrated itself through many hierarchal levels of organization throughout the biological world. From genes to organs to individuals to species, variation can be seen at every level. The processes that regulate variation at specific levels subsequently dictate what phenotypic changes will result. Most importantly, changes in developmental processes have contributed greatly to morphological innovations that are seen today. This paper will seek to explore the effects of changes in developmental genetics on the generation and accommodation of evolutionary novelties, while exploring the highly integrative and complex system of development from which that phenotypic change results.

Perspective determines how evolution is defined. In the case of species selection (depending on what evolutionary time scale is selected), the creation and divergence of a particular species could be viewed as gradual or punctuated. Similar to species selection, variation generated within an individual can be seen in the same light. In the early twentieth century, Goldschmidt took on the challenge of denoting effect of mutation size on phenotypic change. He valued developmental processes in his understanding of mutational changes, allowing the possibility of one mutation to create a new evolutionary form, stabilized by orthogenetic development, variation directed by fixed goals (Goldschmidt, 1933). Twenty years later, Simpson proposed a contradictory statement to Goldschmidt's theory of mutational changes. Simpson promoted the idea that evolution was a consequence of small, abundant,

accumulated mutations that correspond to large phenotypic changes (Simpson, 1953). Unlike Goldschmidt, Simpson discounted development in his description of phenotypic change and placed greater importance on the more frequent, smaller mutational changes, claiming that larger mutations have more deleterious effects on the organism (Simpson, 1953). As mentioned before, these theories of evolutionary novelties were predicated on the basis of assumptions and what little was known of the fossil record. Simpson stood strong in his belief that intermediaries must exist between morphological states (Simpson, 1953). On the contrary, there are instances where small mutational accumulations would not explain certain morphological innovations. An example of this would be the manifestation of eye translocation during a specific embryonic stage that occurs in flounders, along with the asymmetric morphologies of its skull and muscles (Goldschmidt, 1953). According to Goldschmidt, only a single step was required to start the eye migration, and all of the other transformations (muscles, skull, fins) were subsequent effects of the first (Goldschmidt, 1953).

The magnitude of phenotypic effects are related to the timing of gene expression during embryonic development. Development is an integrated process that relies upon highly conserved regulatory genes that play a large role in determining the body plan (Abouheif, 1997). Small genetic changes can produce drastic morphological effects when implemented early on in embryogenesis (de Beer, 1951). "Embryogenesis may appear quite deterministic on a macroscopic scale; however, at the cellular level events proceed in a more stochastic fashion. It is only the aggregate behavior that exhibits overall coordination (Oster and Alberch, 1982)." So

now we ask, if development is a highly integrated, conserved, complex program, how can such drastic "stochastic" variations arise and persist throughout evolutionary time?

Modularity and degeneracy allow changes to occur in the developmental program, despite high levels of evolutionary conservation (McCune, 2014). This quasi-dissociability permits heterochrony which can modify the growth rate of a skull without altering the rate of growth of the body (McCune, 2014). Modularity also allows co-option and exaptation to occur, which can subsequently lead to the generation of novel structures (i.e., feathers originally formed for thermoregulation, eventually co-opted for flight) (McCune, 2014). Degeneracy allows genes to react differently to selective pressures while yielding the same output (Edelman and Gally, 2001). An example of degeneracy is found in the third codon position—a slight change in the third base pair will most likely result in the production of the same amino acid (Edelman and Gally, 2001). Because degeneracy can respond to variable pressures, they are quite adaptable, and thus accommodate changes in an integrated organism (McCune, 2014). Take Slijper's goat for example, a goat born without forelimbs that learned to be bipedal. The phenotypic effects of this developmental change yielded an S-shaped spine and larger vertebrae shapes, in addition to inherent properties of the musculo-skeletal system—muscles bigger with use, and bones growing along lines of compression (McCune, 2014). All of these effects were phenotypic, i.e. they weren't genetically determined. Why did this happen?

Exploratory mechanisms accommodate change well and promote diversity. They dispel the notion to have corresponding mutations in separate systems to achieve new functional interactions (Kirschner and Gerhart, 1998). Instead, variation precedes selection, allowing the

process to have a large number of configurations in response to stabilizers (Kirschner and Gerhart, 1998). In the case of Slijper's goat, the musculo-skeletal system responded to the change in morphology, which caused this limb modification to be functional. Through a process of angiogenesis, capillaries will grow towards oxygen deficient cells (McCune, 2014). This process is not genetically determined, but instead will help accommodate any perturbations in morphology (ie, multiple mutations in separate systems are not necessary to accommodate change).

Exploratory mechanisms are cornerstones of evolvability, "an organisms's capacity to generate heritable phenotypic variation (Kirschner and Gerhart, 1998)." The versatility of proteins increases flexibility of physiological processes, which also promotes evolvability in organisms (Kirschner and Gerhart, 1998). One example of this is calmodulin, a highly conserved inhibitor that regulates many cellular processes. Its ability to bind to a diverse number of sequence targets enables it to embody various configurations to perform different functions (Kirschner and Gerhart, 1998). Like exploratory mechanisms, protein versatility decreases the need for multiple mutations needed for new regulatory interactions (Kirschner and Gerhart, 1998).

But all of this wouldn't be possible without the fundamental protein code, Hox genes. Hox genes provide the genetic "toolkit" which regulates the development of various structures (Shubin and Marshall, 2000). These genes are deployed sequentially—their location in the genome corresponds to its segment identity where they are regionally expressed along the anterior-posterior axis of the embryo (Patel, 2014). Mutations that occur within the Hox gene

region can generate substantial phenotypic effects, even if they are small mutations (Shubin and Marshall, 2000). Gene duplications of any part of the Hox cluster will subsequently duplicate regulatory elements, which will promote variation (Shubin and Marshall, 2000). Regulatory elements, like transcription factors, can activate or repress transcription to dictate levels of gene expression. Gene duplication can also lead to co-option. Initially, the genes would be redundant, but given evolutionary time, coding region function would diverge and diversify, thereby increasing variation (Kirschner and Gerhart, 1998).

Developmental genetic data cannot only be used to explain the appearance of variation within a population, but also to explain phylogentic relationships between character traits. Shared regulatory pathways and gene expression are evidence for homology (Abouheif, 1997). The debate over the *Pax6* gene of mice seeks to define whether or not it is homologous to the *eyeless* gene of Drosopilia due to the difference in eye morphology. Genetic co-option is used to explain the homology of the two genes. Abouheif states that since their biochemical function is conserved, but their developmental function differs, they are still homologous at the gene expression level (Abouheif, 1997).

No two fingerprints are identical. Variation is a byproduct of natural selection acting on mutational changes promoted and accommodated by developmental processes. The magnitude of morphological change is not proportional to the size of the genetic mutation that created it. Everything interacts with one another on different hierarchal levels, contributing to the overall diversity that is expressed in the natural world. In the words of Darwin, "It is not the strongest, or the most intelligent who will survive, but those who can best manage change."

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