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The proper place of hopeful monsters in evolutionary biology

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Abstract

Hopeful monsters are organisms with a profound mutant phenotype that have the potential to establish a new evolutionary lineage. The Synthetic Theory of evolutionary biology has rejected the evolutionary relevance of hopeful monsters, but could not fully explain the mechanism and mode of macroevolution. On the other hand, several lines of evidence suggest that hopeful monsters played an important role during the origin of key innovations and novel body plans by saltational rather than gradual evolution. Homeotic mutants are identified as an especially promising class of hopeful monsters. Examples for animal and plant lineages that may have originated as hopeful monsters are given. Nevertheless, a brief review of the history of the concept of hopeful monsters reveals that it needs refinements and empirical tests if it is to be a useful addition to evolutionary biology. While evolutionary biology is traditionally zoocentric, hopeful monsters might be more relevant for plant than for animal evolution. Even though during recent years developmental genetics has provided detailed knowledge about how hopeful monsters can originate in the first place, we know almost nothing about their performance in natural populations and thus the ultimate difference between hopeful and hopeless. Studying the fitness of candidate hopeful monsters (suitable mutants with profound phenotype) in natural habitats thus remains a considerable challenge for the future.

Keywords: Gradualism; Homeosis; Macroevolution; Synthetic theory; Saltational evolution

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Introduction: navigating evolutionary biology through the Skylla of gradualism and the Charybdis of intelligent design

Our planet is inhabited by an impressive number of incredibly complex and diverse organisms, such as plants and animals (including human beings). Compared to the complexity of, say, the human body, even the Space Shuttle looks quite poor, and the diversity of insects alone is just breathtaking. Explaining exactly how the great complexity and diversity of life on earth originated is still an enormous scientific challenge (Carroll, 2001). It may first appear unnecessary to point out that the scientific method has to be brought to bear on the problem. In addition to the inherent biological complexity of the problem, however, I currently see two other major obstacles for future progress from a heuristic perspective that may justify such a remark:

(i) There is the widespread attitude in the scientific community that, despite some problems in detail, textbook accounts on evolution have essentially solved the problem already. In my view, this is not quite correct.
(ii) There is the opposite view gaining ground mainly outside of scientific circles that living organisms are so complex that they must have been created by an external intelligence – a novel version of creationism known as ‘‘Intelligent Design’’ (ID). A philosophical analysis of whether ID is a scientific hypothesis at all is beyond the scope of this review. In any case, its ability to develop fruitful research programs has remained negligible so far (Raff, 2005). With few exceptions (e.g., see Lönnig, 2004, and references cited therein) biologists do not consider ID helpful in our endeavour to explain life’s complexity and diversity.

This does not mean, however, that we already have a complete and satisfactory theory which explains how the complexity and diversity of life originated. Thus the rejection of ID or other varieties of creationism is not based on the comprehensive explanatory power of any existing evolutionary theory, but has to be considered as an epistemological presupposition and heuristic basis of biology as a natural science. Since we do not have a complete account of the origin of complex organismal features, clarifying their origin arguably remains one of the greatest challenges of biology (Lenski et al., 2003).

All well-supported scientific theories used to explain the complexity and diversity of living beings are variants of evolutionary hypotheses. According to Darwin (1859), evolution is a two-stage process: heritable random variation provides the raw material, natural selection acts as the directing force that leads to the adaptation of organisms to the environment. By uniting the classical observations of morphology, systematics, biogeography and embryology with population genetics the ‘‘Synthetic Theory’’ (or ‘‘Modern Synthesis’’) of evolutionary biology was developed during the 1930s and 1940s (Dobzhansky, 1937; Mayr, 1942; Simpson, 1944; Mayr and Provine, 1980; Reif et al., 2000; Junker and Hoßfeld, 2001; Junker, 2004). The Synthetic Theory considers evolution usually as the result of changes in allele frequency due to natural selection that engender subtle modifications of phenotype. Like Darwin the Synthetic Theory argues that evolution occurs always gradually, and that complex and unique structures evolve through "an almost infinite number of generations" subject to natural selection fine-tuning these traits. In time, such gradual changes accumulate and result in large differences unique to higher taxa. Gradualism, that evolution proceeds by very small steps and this way creates the unique traits at all levels of biological diversity, can be seen as a central tenet of Darwin and the Synthetic Theory. According to this view, the gradual process of evolution by natural selection that operates within populations and species (often termed microevolution) also creates the unique traits recognizable at higher taxonomic levels (often termed macroevolution).

Macroevolution is usually defined as evolution at and above the species level. Speciation, however, can go along with almost no structural and functional changes, while even within species, there can be dramatic morphological differences (e.g., maize vs. teosinte, see below). In the following I will use the term macroevolution in a more narrow sense only for those evolutionary processes that bring about innovations (or novelties), or changes in body plans. Even in this terminology the Synthetic Theory maintains that macroevolution is just microevolution extended over large periods of time.

Despite all its indisputable explanatory power, the Synthetic Theory has serious shortcomings (Wagner, 2000). The empirical basis of gradualism is weak at best. The most direct view into life's past on earth is provided by the fossil record. With its abrupt transitions, however, it provides little evidence for a gradual evolution of new forms (Gould and Eldredge, 1993). Also the branching patterns of higher taxa in both animals and plants as revealed by cladistics and systematics do not support the idea that the major features of body plans and their constituent parts arose in a gradual way (Vergara-Silva, 2003). Moreover, even though population genetics might be the most elaborate approach that we have to explain evolution, it might not be sufficient. For example, it falls short of explaining innovations and constraints, and the evolution of body plans (Riedl, 1977; Gilbert et al., 1996; Wagner, 2000; Haag and True, 2001; Wagner and Müller, 2002; Wagner and Laubichler, 2004). Why did bacteria not just give rise to more and more optimized and better and better adapted bacteria forever, but to mushrooms, monkeyflowers and man? In fact, population genetics tells us little about the mechanisms by which changes in a linear sequence of nucleotides that constitutes the genomes of living organisms produces the diversity and complexity of life (Weiss, 2005). Changes in allele frequency within populations are certainly of great importance for understanding evolution and the origin of biodiversity, but they are by far not sufficient, because the number of genetic loci is not fixed in evolution (e.g., animals and plants have roughly about 10 times more genes than bacteria). New genes originate during evolution by processes such as gene, chromosome or whole genome duplications, and genes can lose their function and even get lost, e.g. by deleterious mutations. The birth and death of genes as well as changes in regulatory or genetic interactions between existing genes are of special importance during the evolutionary origin of key innovations and novelties (Theißen, 2002, 2005).

In addition to explanatory deficits the Synthetic Theory also has philosophical shortcomings. By maintaining that evolution must be gradual and that macroevolutionary patterns can be fully explained by the action of natural selection and adaptation to the environment alone, the Synthetic Theory made over-extended claims, and hence left the realm of science and developed into an ideology (Wagner and Laubichler, 2004). We should not forget, however, that all scientific knowledge is hypothetical and preliminary, and that there is no reason why this should not also apply to scientific explanations of the complexity and diversity of life. That all forms of life originated in a gradual way, therefore, might be considered an extremely interesting hypothesis, but in the natural sciences there is no such thing as a proven fact.

So in its quest to explain the origin of complex organisms on our planet, evolutionary biology should remember its basic principles. Within this framework it should, however, also be more tolerant towards alternative views. The vast majority of biologists will agree that evolution is inevitable when a few conditions are met: replication, variation (mutation), and differential fitness (competition) (Dennett, 2002). But while these principles might easily explain how any kind of organism gives rise to an optimized organism (concerning whatever criteria), it is hard to see how it explains the origin of e.g. eukaryotes, plants and animals from prokaroytes. Studies of digital organisms suggest that complex functions can originate by random mutation and natural selection (Lenski et al., 2003), but the extent to which such in silico studies reflect evolutionary events in living organisms remains unclear.

Insights into the developmental genetics of multicellular organisms as well as the fossil record suggest that evolution can be saltational rather than gradual. For many years, however, the traditional population-genetic tenets of the Synthetic Theory made impossible a serious discussion of saltational mechanisms as explanations of macroevolutionary change (Vergara-Silva, 2003). But given the problems the Synthetic Theory faces in explaining the modes and mechanisms of macroevolution biology should also consider alternative mechanisms, as long as they are accessible by scientific methods.

Here I argue that saltational evolution occurred, and that "hopeful monsters" might have acted as first steps in this process. I briefly review the short but controversial history of the concept of hopeful monsters, and outline that, if it is to be a useful addition to evolutionary biology, it needs both conceptual refinements and empirical tests.

Hopeful monsters: Goldschmidt's legacy

The term "hopeful monster" was introduced by Richard Goldschmidt decades ago. Goldschmidt saw true species separated by "bridgeless gaps" that could only be overcome by saltational changes, and not by the slow gradual changes envisaged by Darwin and the Synthetic Theory. In order to explain the origin of species, therefore, Goldschmidt (1940) developed views that broke sharply with the Synthetic Theory (reviewed by Dietrich, 2000, 2003). While he raised no objection to gradual and continuous change within species, he argued that new species arise abruptly by discontinuous variation, or macromutation. Goldschmidt was aware that the vast majority of macromutations have disastrous effects on the fitness of organisms – these he called "monsters". But in Goldschmidt's view every once in a while a "hopeful monster" is generated which is adapted to a new mode of life. According to Goldschmidt, macroevolution proceeds by the rare success of these hopeful monsters rather than by an accumulation of small changes within populations.

Goldschmidt (1940) presented two mechanisms for how "hopeful monsters" might originate. The first one is based on "developmental macromutations" in "rate genes" or "controlling genes" that change early development and hence cause large effects in the adult phenotype. While these kinds of mutations were based on the classical gene concept, Goldschmidt rejected the classical model of the gene in the second mechanism, and developed an alternative model in which systemic rearrangements of chromosomes ("systemic mutations") could produce new developmental systems and potentially new species quickly. Goldschmidt's idea of hopeful monsters was not tied to his idea of systemic mutations, but he used the possibility of mutations in developmentally important genes to make the genetic mechanism of systemic mutation more plausible. According to Dietrich (2003) it was his rejection of the classical gene concept even more than his views on saltational evolution via hopeful monsters that damaged Goldschmidt's scientific reputation and, to some extent, also the credibility of hopeful monsters.

Hopeless monsters: the Synthetic Theory strikes back

Goldschmidt's ideas about developmentally important mutants with large effects were not met with the same hostility as his views on systemic mutations (Dietrich, 2003). However, he did not succeed in establishing hopeful monsters as an accepted addition to evolutionary theory. Representatives of the Synthetic Theory saw the accumulating evidence of the evolutionary importance of selection on many mutations of small effect and differentiation at the population level as indication that there is no need for hopeful monsters in evolutionary biology (Dietrich, 2003). For Simpson (1944) homeotic mutants were insufficient to explain the distinction between microevolution and macroevolution. Wright (1941) and Simpson (1944) raised a number of objections to Goldschmidt's views about the evolutionary importance of drastic mutants, e.g. that, like any other mutant, they do not create new species, and that the appearance of a mutant individual is not evolution. To whom, for example, shall hopeful monsters mate? All its relatives are very different from it, arguably even members of another species. And the chance that organisms with reasonable fitness were generated rather than "hopeless monsters" was considered to be very low. In simple models the fitness of an organism decreases proportionally to its deviation from the wild type. It can thus be assumed that profound phenotypic transformations undermine the fitness of the affected organisms in such a serious way that there is always strong selection against them (reviewed by Svensson, 2004). Thus from a population genetics point of view, hopeful monsters appeared impossible. Not long after Richard Goldschmidt's brainchild had entered the world of ideas in evolutionary biology, therefore, hopeful monsters were generally considered a hopeless case. It is still widely believed that any mutation of major effect is unlikely to be tolerated by natural selection and thus generates ''hopeless'' rather than hopeful monsters (Akam, 1998).

Helpful monsters: homeotic mutants enter the evo-devo stage

Hopeful monsters remained anathema as long as theoretical population genetic models dominated evolutionary biology and developmental biology remained a neglected topic. The situation changed, however, mainly due to quantitative trait loci (QTL) analyses of real differences between closely related organisms, and the ongoing reintegration of developmental biology into evolutionary biology.

In recent years QTL analyses revealed that novel morphological forms in evolution may result from changes in just a few genes of large effect. The most intensely studied case in plants is the domestication of maize (*Zea mays*. ssp. *mays*) from teosinte (*Zea mays* ssp. *parviglumis*). During this process the female inflorescence (''ear'') of corn originated as an unprecedented novelty due to changes at just about five gene loci (Doebley et al., 1997; Wang et al., 1999; Wang et al., 2005). It has been argued that the selection regime during domestication is very different from that of evolution in the wild. But QTL analyses of naturally occurring polymorphisms affecting flower and inflorescence structures corroborated the view that even drastic structural changes can be based on mutations at just one or a few genetic loci (see, e.g., Gailing and Bachmann, 2000; Moritz and Kadereit, 2001).

Major deficiencies in the Synthetic Theory, e.g. in explaining evolutionary novelties and constraints, led to the reintegration of developmental biology into evolutionary biology, giving rise to ''evolutionary developmental biology'' (''evo-devo'', for short). The evo-devo rationale takes into consideration that multicellular organisms usually develop from single cells (zygotes) in each generation anew. This implies that morphological changes in evolution occur by changes in developmental processes. Since development is largely under genetic ''control'', novel morphological forms in evolution frequently result from changes in developmental control genes. Thus evo-devo projects often study the phylogeny of developmental control genes and their role in the evolution of morphological features (for details of the evo-devo rationale, see Gould, 1977b; Gilbert et al., 1996; Theißen et al., 2000; Carroll, 2001; Arthur, 2002).

In recent years much progress has been made in understanding the genetic mechanisms that bring about drastic yet coordinate changes in the adult phenotype by modification of development. Changes in both the timing (heterochrony) and the position (heterotopy) of developmental processes can occur. In the case of plants, however, heterotopy and heterochrony are often difficult to distinguish, because plants develop continuously, so shifting developmental events later or earlier during plant life may lead directly to a change in the position of the structure generated by the developmental program (Kellogg, 2000). Quite a number of evolutionary novelties and characteristics of major clades – many of which have been used for decades as taxonomic characters—can be explained as the result of heterotopy or heterochrony, underscoring its importance for macroevolution (Kellogg, 2000).

An important subset of heterotopic changes are homeotic transitions (Baum and Donoghue, 2002). The term ''homeosis'' had been coined by William Bateson in 1894 to describe a type of variation in which ''something has been changed into the likeness of something else'' (Lewis, 1994). Well-known examples are provided by the fruit fly *Drosophila melanogaster*, such as the *Antennapedia* mutant, which has antennae replaced by leg-like organs, or two mutants studied by Richard Goldschmidt, *podoptera*, with transformation of wings into leg-like structures, and *tetraltera*, with transformation of wings into halteres (reviewed by Dietrich, 2000). Homeotic mutants are also frequent in plants, affecting both vegetative and reproductive organs (Sattler, 1988; Meyerowitz et al., 1989). Especially well known are floral homeotic mutants, i.e. mutant plants with flowers that have more or less normal floral organs in places where organs of another type are typically found.

Many flowers consist of four different types of organs which are arranged in four whorls: sepals, petals, stamens and carpels. In the model plant thale cress (*Arabidopsis thaliana*) homeotic mutants can be categorized into three classes: A, B and C. Ideal class A mutants have carpels in the first whorl instead of sepals, and stamens in the second whorl instead of petals. Class B mutants have sepals rather than petals in the second and carpels rather than stamens in the third whorl. And class C mutants have flowers in which reproductive organs (stamens and carpels) are replaced by perianth organs (petals and sepals, respectively), and in which the determinacy of floral growth is lost, resulting in an increased number of floral organs (Meyerowitz et al., 1989; Theißen, 2001). Such ''filled flowers'' are well known from many wild and ornamental plants, including *Arabidopsis*, *Antirrhinum*, *Rosa* (rose), *Prunus* (e.g., cherry), *Petunia* and *Tulipa* (tulip) (Fig. 1B).

The defined classes of homeotic mutants are explained by simple combinatorial models such as the ABC model of flower development (reviewed by Theißen, 2001). It proposes three different floral homeotic functions to explain how the different floral organs adopt their unique identities during development. These functions are termed A, B and C, with A specifying sepals in the first floral whorl, A + B petals in the second whorl, B + C stamens in the third whorl and C carpels in the fourth whorl.

Cloning of homeotic genes during the 1980s and 1990s in both animals and plants revealed that they all encode transcription factors, i.e. proteins that recognize specific DNA motifs of other genes and influence their transcription. While the homeotic genes of animals encode homeodomain proteins, the vast majority of homeotic genes of plants encode MADS-domain proteins (Gehring, 1992; Carroll, 1995; Becker and Theißen, 2003; Theißen, 2001; Meyerowitz, 2002).

Homeotic genes reveal that major developmental events such as the specification of organ identity are often under the control of a limited number of developmental control genes. The analyses of mutants and transgenic organisms demonstrate that

Fig. 1. A putative hopeless (B) and hopeful monster (D). In the upper row, a wild-type flower of tulip (*Tulipa gesneriana*, left) is compared to a "double flower" or "filled flower" mutant (right); while the wild-type flower has male (stamens) and female reproductive organs (carpels) in the centre, the filled flower is sterile, because all reproductive organs are transformed into showy yet sterile perianth organs, thus hampering sexual reproduction and undermining fitness. The lower part shows inflorescences of Shepherd's purse (*Capsella bursa-pastoris*). While wild-type flowers have four different types of floral organs including petals (the white organs in C), all petals are transformed into stamens in the "decandric" variety shown in D, which hence has 10 stamens and 2 carpels in all of its flowers and is fully fertile. Note that while evolutionary biology usually favours animal model systems (an attitude known as zoocentrism), the insects shown here are only decorative elements. (Pictures courtesy of Hannelore Simon (upper row) and Janine Ziermann (lower row)).

changes in these loci can bring about profound, yet coordinated morphological changes. Some of the mutant phenotypes (e.g., petaloid rather than sepaloid 1st whorl floral organs, actinomorphic rather than zygomorphic flowers, four-winged rather than two-winged flies), resemble differences in character states between major organismic lineages. There is a long debate going on as to whether the genes underlying such ''phylomimicking mutants'' (Haag and True, 2001) define loci that play an important role in character changes during macroevolution.

As a matter of fact, changes in the expression domains of floral homeotic genes in mutant or transgenic plants can bring about homeotic transformations of floral organs. For example, the expression of class C genes in the whorls of the perianth leads to a transformation of sepals into carpelloid organs and of petals into staminoid organs (Bradley et al., 1993). Similarly, the ectopic expression of class B genes in the 1st and 4th floral whorls of *Arabidopsis* leads to a transformation of sepals into petaloid organs and of carpels into staminoid organs (Krizek and Meyerowitz, 1996). A survey during the course of evo-devo projects suggested that these changes do not only underlie short-lived transgenic and mutant plants, but also natural morphological diversity generated during macroevolution, and thus are suitable models for evolutionary processes. For example, tulips (*Tulipa gesneriana*) and other lily like plants (Liliaceae) have flowers displaying organ identities quite similar to the ones of higher eudicots, but first whorl organs are typically petaloid like second whorl organs rather than sepaloid (Fig. 1A). This suggests that a homeotic transition in the first floral whorl from sepaloid to petaloid organ identity, or vice versa, occurred during the evolution of flowering plants. Petaloid organ identity requires the function of class B floral homeotic genes. Indeed, when class B genes were investigated in tulip, they were found to be expressed not only in the petaloid tepals of the second floral whorl, but also in the organs of similar identity in the first whorl (Kanno et al., 2003). Similar examples are provided by many flowers of the basal eudicot family Ranunculaceae, which have distinctly different petaloid organs in the first two whorls. Expression studies suggested that petaloidy of 1st whorl organs is due to a shift of class B gene expression towards the 1st floral whorl (Kramer et al., 2003).

These findings support the view that shifts in the boundaries of class B floral homeotic gene expression that brought about floral homeotic changes contributed to the diversity of floral architecture. They add to a growing stream of reasoning fuelled by evolutionary analyses of morphological characters, all indicating that homeosis played a significant role in plant evolution. For example, Sattler (1988) reviewed putative cases of homeosis in the evolution of flowering plants from the cellular to the organismic level, including several affecting vegetative organs such as leaves and leaflets. The origin of maize from teosinte with its dramatic changes that gave rise to the female inflorescence (''ear'') of maize has traditionally invited scientists to explain it involving dramatic, even ''catastrophic'' events such as homeosis (Iltis, 1983, 2000). Kellogg (2000) summarized evidence for the importance of heterotopy during the evolution of grasses (Poaceae); examples include the evolution of the unique epidermal morphology of grasses, the origin of the grass flower and spikelet, the formation of unisexual flowers in the panicoid grasses and the repeated origin of

C4 photosynthesis. In contrast, heterochrony may underlie the novel morphology of the grass embryo (Kellogg, 2000). Ronse De Craene (2003) provided morphological evidence for the evolutionary significance of homeosis in the flowers of diverse angiosperms, such as Rosaceae, Papaveraceae and *Lacandonia*. For example, there is strong phylogenetic and morphological evidence that the petals of the Rosaceae (comprising well-known cultivated plants such as roses, strawberries and apples) were derived from stamens (Ronse De Craene, 2003). Baum and Donoghue (2002) reconsidered the concept of "transference of function" during plant evolution, including many putative cases of homeosis. Models of how evolutionary variation of the ABC system of floral organ identity specification could explain floral diversification during evolution have been provided e.g. by Theißen et al. (2000) and Kramer et al. (2003). Rudall and Bateman (2002, 2003) described different kinds of teratological plants with peloric flowers, especially in orchids and the mint family, which can be understood in terms of heterotopy and homeosis. Rutishauser and Isler (2001) and Rutishauser and Moline (2005) considered homeosis or even more radical concepts such as "fuzzy morphology" and "continuum morphology" to explain at least some of the extreme peculiarities in the body plans of bladderworts (*Utricularia*) and river-weeds (Podostemaceae), respectively.

It is maybe not by chance that all these examples represent plants. It could well be that the more "open" structure and additive mode of growth of plants implies that homeotic mutations are more important in plant than in animal evolution. However, evidence for homeotic shifts in animal evolution is not completely lacking. An instructive example is the digits in the bird hand, which was inferred by conflicts in homology assignments. Traditional criteria for recognizing homologous features include structural similarity, position within a comparable set of features, and the existence of transitional forms between presumptive homologues, either in development (ontogeny) or evolution (as revealed by the fossil record) (Rutishauser and Isler, 2001; Theißen, 2005; and references therein). The appendages of many tetrapods have 5 digits, while bird wings have just 3. The digits of the wings of birds are considered on embryological grounds to be digits 2, 3, and 4, while phylogenetic analyses of fossil data indicate that birds descended from theropod dinosaurs that had lost digits 4 and 5 and thus have digits 1, 2, 3. But how can it be that 1,2,3 = 2,3,4? Wagner and Gauthier (1999) suggested that a homeotic transformation occurred, so that now e.g. a digit developing at position 2 has the organ identity (or "special quality") of an position 1 organ (hence "2 = 1"). Expression studies of Hox genes determining digit identity are compatible with this hypothesis, although alternative explanations remain conceivable (Vargas and Fallon, 2005). The hands of kiwis and tyrannosaurs could represent further cases of natural homeotic transformation of digits (Wagner and Gauthier, 1999).

Taken together, there is increasing evidence, mainly from plants, but also from animals, that homeotic transitions have indeed occurred during evolution, and that these are based on mutations in just one or a few genetic loci.

In principle, homeotic changes could occur in a gradual mode of evolution (Sattler, 1988). However, given that full conversions in organ identity usually take place in a mutant individual just by the mutation of a single homeotic gene, a saltational mode of character change appears more plausible, at least from a genetic point of view. This, however, would be contradictory to the assumption of the Synthetic Theory that all kinds of evolution are gradual and based on changes in allele frequency at many loci. And it would have a quite dramatic consequence: homeotic mutants should represent important steps during a macroevolutionary transition. Since homeotic mutants can be considered as profound variants of any organismic design, they might reasonably be called hopeful monsters. Remarkably, Goldschmidt already studied homeotic mutants in the fruit fly *Drosophila* such as *podoptera* and *tetraltera* because he considered them as excellent candidates for hopeful monsters (reviewed by Dietrich, 2000, 2003). But now evo-devo has increased the evolutionary credibility of drastic "saltational", yet coordinated morphological changes as represented by floral homeotic transitions (Bateman and DiMichele, 2002; Kramer et al., 2003; Theißen et al., 2000; Theißen et al., 2002). Thus, thanks to the "helpful monsters" (Coen, 2001) provided by developmental genetics, hopeful monsters are back on the centre stage of evolutionary biology.

The return of hopeful monsters

The concept of hopeful monsters would have remained as dead as a Dodo if any orthodox evolutionary theory could fully explain the origin and diversification of life as we know it. But there is no such comprehensive theory, and in their attempts to fill the gaps of existing ones, not only has evo-devo developed, hopeful monsters have also been reconsidered several times.

In a kind of Goldschmidt variation Gould (1977a) argued that the fossil record provides very little evidence for a gradualistic mode of macroevolution, because the transitions between major groups of organisms are characteristically abrupt. This observation is usually attributed to the notorious incompleteness of the fossil record, but with increasing sampling and intensifying study of the fossil record it is becoming less and less convincing (Gould and Eldredge, 1993). Even more important is the notion that there are many cases of macroevolutionary events for which a reasonable story of continuous change cannot be constructed (Gould, 1977a). Using the phrase "what good is half a wing?" Gould (1977a) outlined that in quite a few cases intermediate stages might have had a function different from the final structure (e.g., the "half wing" may have helped in trapping prey or controlling body temperature), a concept termed "preadaptation". According to Gould (1977a), however, in many cases gradualism cannot be saved that way. For example, on the island of Mauritius two genera of snakes share a feature present in no other terrestrial vertebrate, namely splitting of the maxillary bone of the upper jaw into front and rear halves connected by a moveable joint. "How can a jawbone be half broken" (Gould, 1977a)? A detailed consideration of the case rejected every preadaptive possibility that came to mind in favour of a discontinuous transition (Frazzetta, 1970). This and other cases led Gould (1977a) to accept the occurrence of discontinuous transitions ("saltation") in macroevolution. According to this view, the absence of intermediate forms does not simply reflect the incompleteness of the fossil record, but often the true lack of such forms.

Following Darwin's friend Thomas Henry Huxley, Gould (1977a) argued that gradualism is not a necessary corollary of evolution by natural selection, and that it is therefore unnecessary that it became the central tenet of the Synthetic Theory. He suggested that the saltational change of the hopeful monster may not produce a perfect form all at once, but rather may serve as a "key" adaptation to shift its possessor towards a new mode of life. In a second phase a large set of collateral alterations may arise in a more traditional, gradual way once the key innovation forces a profound shift in selective pressures. Gould (1977a, b) agreed with Goldschmidt that major evolutionary transitions may be accomplished by small alterations in the rate of early development that accumulate through growth to yield profound differences among adults.

Gould (1977a) predicted that Goldschmidt's ideas about evolution will be largely vindicated in the world of evolutionary biology during the 1980s. As we all know, he was wrong. However, hopeful monsters were in detail revisited by Bateman and DiMichele (1994, 2002) in their concept of "neoGoldschmidtian saltation". We owe to these authors the first detailed elaboration of a scientific concept of hopeful monsters. The authors defined saltational evolution as a genetic modification that is expressed as a profound phenotypic change across a single generation and results in a potentially independent lineage that they termed "prospecies". These prospecies are just Goldschmidt's hopeful monsters by another name (which is why the term is not adopted here). Bateman and DiMichele (1994, 2002) discuss several putative mechanisms of saltational evolution, and how they could bring about speciation and profound phenotypic novelties. Studying fossil seed-ferns and extant orchids Bateman and colleagues realized that vast numbers of hopeful monsters are generated continuously by heterotopy (including homeosis) and heterochrony due to mutations in key developmental genes that control morphogenesis (Bateman and DiMichele, 2002; Rudall and Bateman, 2002, 2003). The authors assume that the fitness of the hopeful monsters thus generated is, at least in most cases, too low to survive competition-mediated selection. They conclude that the establishment of hopeful monsters is most likely under temporary release from selection in environments of low biotic competition for resources, followed by honing to competitive fitness by gradual reintroduction to neoDarwinian selection. Bateman and DiMichele (2002) conclude their considerations by the catchy statement that evolution equals phyletic gradualism in DNA sequences plus punctuated equilibria in morphology. (Phyletic gradualism refers to the often almost "molecular clock"-like changes in DNA sequences but thus ignores that genenetic changes can also be punctuated, e.g. in the case of gene, chromosome or even genome duplications).

In addition to these conceptual considerations hopeful monsters have been considered as reasonable hypotheses in individual cases of macroevolution where scenarios of gradual evolution appeared implausible. Arguably the most striking case is provided by the origin of turtles (Testudines). Turtles have the most unusual body plans of the amniotes, with a dorsal shell consisting of modified ribs (Fig. 2A). Ventral ribs are not formed, instead the dermal plastron covers the ventral body.

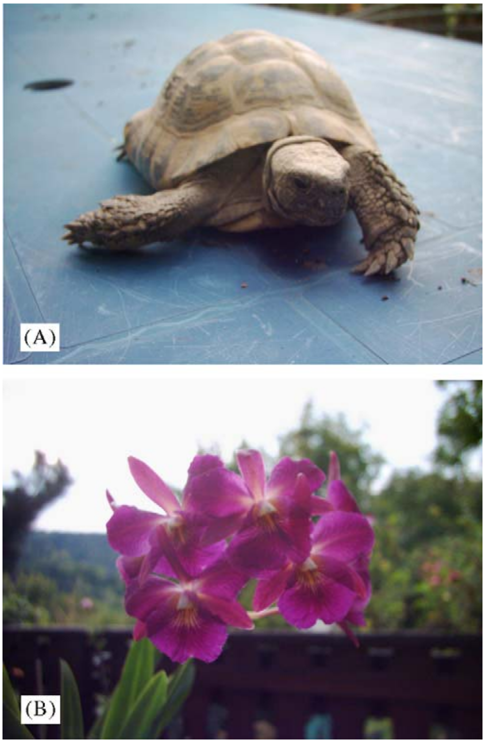

Fig. 2. Putative descendants of hopeful monsters. (A) Turtles (*Testudo hermannii*) and (B) flowering plants (inflorescence of an orchid species) are prime candidates for owing their body plans to saltational evolution via hopeful monsters rather than the gradual evolution envisaged by the Synthetic Theory.

Moreover, in contrast to the situation in other vertebrate species in which the scapula develops outside the rib cage, the shoulder girdle is found inside the rib cage in turtles (Rieppel, 2001). For such a situation a plausible scenario of continuous change from any kind of possible ancestor cannot be constructed (Rieppel, 2001). In line with this, turtles appear abruptly in the fossil record of the late Triassic, with no intermediate changes so far being found (reviewed by Ohya et al., 2005). Even though this does not completely rule out that many intermediate forms once existed, it at least suggests that the turtle body plan originated quickly, especially since one cannot say that turtle bones have a low potential to fossilize (a serious problem in other cases of rapid appearance of novelties, e.g. origin of flowers, see below). There is meanwhile evidence that the turtle body plan originated due to changes in axial-level specific alteration in early development, caused by changes in the expression domain of some *Hox* genes (Ohya et al., 2005).

Due to their striking evolution, Rieppel (2001) considered ‘‘turtles as hopeful monsters’’. However, turtles have a fossil record dating back more than 200 million years and are widespread in many parts of the world, with a number of species found in some of the driest deserts and the deepest seas. Turtles are thus neither monsters nor just hopeful, but well adapted and successful organisms. It would be more appropriate to say, therefore, that turtles are descendants of hopeful monsters rather than hopeful monsters themselves.

Cambrian explosion and abominable mystery: hoping for hopeful monsters

We have already seen that in some cases, such as the turtle body plan, there is evidence that saltational events such as homeotic transitions contributed to the origin of evolutionary novelties. But how important have these events been for global biodiversity? In principle they could represent exceptional cases that do not justify a general revision of evolutionary biology. But this is probably far from the truth.

The structural diversity of multicellular organisms on our planet appears to have originated to a large extent in two major ''bursts''. The fossil record suggests that during the ''Cambrian Explosion'' about 540 million years ago the visible body plans of (almost) all animal taxa (extant and extinct) originated within a few million years (Philippe et al., 1994; Fortey et al., 1997; Valentine et al., 1999). This does not necessarily mean, however, that the respective animal clades also originated during that time; some molecular surveys of animal phylogeny suggest an extended but cryptic Precambrian history of metazoans (Wray et al., 1996; Levinton et al., 2004). This would be in line with the notion of Bateman and DiMichele (2002) that evolution equals phyletic gradualism in DNA sequences (including cladogenesis) plus punctuated equilibria in morphology, and it would require an explanation of how gradually changing genes can bring about saltational changes in morphology. The hypothetical answer favoured here is that changes in just a limited number of developmental control genes generating ''hopeful monsters'' are sometimes key to morphological transitions, while the vast majority of the genome may change more or less in a clock-like way with not much impact on the origin of morphological novelties and the evolution of body plans. Anyway, in many respects, such as number of species, the insects, which originated in the Carboniferous, became by far the most successful group of animals (Carroll, 2001).

More than 300 million years after the ''Cambrian explosion'', in the late Jurassic or early Cretaceous, the origin and diversification of the flowering plants (angiosperms) provided the second example of an apparently ''sudden'' origin and rapid early morphological radiation. The origin and early diversification of angiosperms was considered an ''abominable mystery'' and ''perplexing phenomenon'' by Charles Darwin about 150 years ago, and has remained a considerable scientific challenge (Crepet, 2000; Theißen et al., 2002; Frohlich, 2003; Frohlich and Parker, 2000; Stuessy, 2004; Theißen and Becker, 2004).

For both the origin of animals and of angiosperms there is no fossil record that would support a gradual mode of evolution, suggesting that saltational events, and hence hopeful monsters, have been involved. Nevertheless, many attempts have been made to explain the origin of diverse animals and angiosperms in a gradualistic way, but conclusive explanations that stood the test of time (including experimental evidence and fossil data) have not been provided. On the contrary, all recent hypotheses about the origin of the flower, for example, postulate critical changes in homeotic genes that brought about e.g. heterotopy or homeosis (Theißen et al., 2002; Theißen and Becker, 2004; Frohlich and Parker, 2000; Frohlich, 2003; Albert et al., 2002). The origin of the angiosperm flower thus became arguably the best studied botanical case of conflict between the Synthetic Theory account and non-gradualistic models of evolutionary key innovations (Vergara-Silva, 2003).

In terms of species and ecological dominance animals and flowering plants became extremely successful groups of organisms. Adaptive radiation and co-evolution between both groups, e.g. due to plant–pollinator and plant–predator interactions, have certainly played a great role in this. But the first steps might have been made by some strange organisms that managed to overcome the developmental constraints of their ancestors and hence acquired key innovations that were the prerequisite for any adaptive radiation and co-evolutionary process that followed.

If animal and angiosperm body plans really originated via hopeful monsters, the importance of hopeful monsters for the biodiversity on our planet can hardly be overestimated.

The future of hopeful monsters

What's in a name? A hopeful monster, by any other name (e.g., prospecies), would remain a remarkable, and controversial, concept. In order to establish hopeful monsters as a useful addition to evolutionary biology, however, the concept has to be refined, and tested empirically.

(a) Thinking in terms of mutually exclusive alternatives has to be overcome. Neither does it appear likely that macroevolution proceeds exclusively by the rare success of hopeful monsters (as assumed by Goldschmidt), nor that it always proceeds by an accumulation of small changes within populations (as maintained by the Synthetic Theory). Rather, the relative importance of both modes of macroevolution has to be determined. This implies that, in contrast to Goldschmidt's views, evolution above and below the species level is not governed by completely different processes, and that both gradual as well as saltational events "bridged" the "gaps" that Goldschmidt saw between species.

(b) Because the importance of saltational evolution might be different in different kinds of organisms, evolutionary biology has to overcome its inordinate fondness for animals. Evolutionary biology has been zoocentric ever since Darwin's time (Bateman and DiMichele, 2002). But animals, with their highly conserved body plans fully outlined during embryogenesis, are arguably the group of organisms in which hopeful monsters are the least likely to appear (but nevertheless, some might have existed, see above). Plants, with their open, additive growth and their great potential for self-fertilization and clonal vegetative reproduction, are much better candidates (Bateman and DiMichele, 2002). So in order to assess the evolutionary importance of hopeful monsters, evolutionary biology has to cover the diversity of life in a less biased way. Possibly Goldschmidt was right in assuming that homeotic mutants are of considerable evolutionary importance, he just might have looked at the wrong species.

(c) It has to be more appreciated that along the contingent trajectories of replicating organisms rarity of events does not necessarily imply unimportance. In natural populations hopeful monsters might be rare (though more frequent than many assume), and successful hopeful monsters might be much rarer still. But even if hopeful monsters are as rare as meteorites that hit the earth, they could be of enormous evolutionary importance. The meteorite that probably wiped out the dinosaurs and many other organisms at the end of the Cretaceous 65 million years ago certainly had an enormous impact on the faunas and floras on earth. But if the Cambrian Explosion or the origin of the angiosperms involved hopeful monsters, they did not have a lesser impact on the biodiversity of our planet.

(d) Putative hopeful monsters have to be experimentally studied and not just discussed. While evo-devo has provided detailed information as to how hopeful monsters can be generated, almost nothing is known about their performance in natural environments. Thus the population dynamics of hopeful monsters has to be studied in extensive field work (Theißen, 2000; Bateman and DiMichele, 2002; Vergara-Silva, 2003; Dietrich, 2003). Non-gradual modes of evolution will not be generally accepted unless a sufficient fitness of hopeful monsters has been documented in natural habitats. Towards that goal, promising candidates for hopeful monsters first have to be identified among extant species. Floral homeotic mutants again appear to be a good study object to us, but of course not every mutant freak will do. Sterile mutants that have transformed their reproductive organs (Fig. 1B) can be readily classified as "hopeless". A good starting point might thus be floral homeotic mutants that appear in populations in the wild, thus revealing at least some minimal fitness. Very few of them have been described, including *bicalyx*, a recessive variety of *Clarkia concinna* (Onagraceae) in which the petals are transformed into sepaloid organs (Ford and Gottlieb, 1992). It occurs only in a small population north of San Francisco (USA), accompanied by a majority of wild-type plants. Another case is a peloric variety of *Linaria vulgaris* that has actinomorphic rather than zygomorphic flowers and persists on a small island near Stockholm (Sweden) (Cubas et al., 1999). While the *bicalyx* gene has not been molecularly characterized so far, it turned out that the *Linaria* variety is affected in a *CYCLOIDEA*-like gene, but by epimutation (methylation of DNA) rather than change in the DNA sequence (Cubas et al., 1999). Both the *Clarkia* and *Linaria* varieties have a very limited range of distribution, and their fitness and competitiveness in the field have not been tested yet, but is questionable (the *Linaria* epimutant may even only propagate vegetatively; Theißen, 2000). In contrast, a floral homeotic variety of Shepherd's purse (*Capsella bursa-pastoris*) has been described for almost 200 years from different locations throughout Europe, and has been documented to exist in populations of considerable size at least for a number of years (Opiz, 1821; Trattinnick, 1821; Murbeck, 1918; Dahlgren, 1919; Gottschalk, 1971; Reichert, 1998). This "decandric" variety has flowers that lack petals (Fig. 1D), since they are all transformed into stamens ("decandric" refers to the fact that the variety has 10 rather than the usual 6 stamens in the wild type). At least in some cases the variety is based on a mutation at a single, co-dominant locus (Dahlgren, 1919). Gottschalk (1971) concluded from the distribution of the floral homeotic variety that it must have a selective advantage compared to the wild type. I am not so sure, but would agree that its fitness is at least not seriously hampered. It thus may qualify as a hopeful monster. Efforts to characterize it in detail, ranging from the molecular genetics of the mutant phenotype to its performance in wild habitats are underway. An important question of future research will be to find out whether epimutations serve as transitional steps in a "trial phase" of mutant phenotypes during the origin of hopeful monsters (Theißen, 2000).

Concluding remarks

We have seen above that hopeful monsters are not just postulated inhabitants of Cambrian faunas and Cretaceous floras, but that they might still be among us, having many proper places in ecological terms ranging from some rock cliffs in California to vineyards in Germany (Ford and Gottlieb, 1992; Reichert, 1998). But, finally, what is the proper place of hopeful monsters in evolutionary biology?

It is dangerous to raise attention to the fact that there is no satisfying explanation for macroevolution. One easily becomes a target of orthodox evolutionary biology and a false friend of proponents of non-scientific concepts. According to the former we already know all the relevant principles that explain the complexity and diversity of life on earth; for the latter science and research will never be able to provide a conclusive explanation, simply because complex life does not have a natural origin.

From a heuristic point of view, both positions are unsatisfactorily. But the habitat of hopeful monsters might be very small. It's the very narrow place between a dogmatic evolutionary biology that accepts only gradual changes, and concepts that maintain that living organisms are too complex to be explained by the scientific method. In other words, the only appropriate place for hopeful monsters in these days is in the small isthmus between the Skylla of dogmatic science and the Charybdis of religious belief. Future progress in evolutionary biology might be a narrow escape.

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