



## SYMPOSIUM ARTICLE

# Phenotypic Plasticity in Vertebrate Dentitions

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**Synopsis** Vertebrates interact directly with food items through their dentition, and these interactions with trophic resources could often feedback to influence tooth structure. Although dentitions are often considered to be a fixed phenotype, there is the potential for environmentally induced phenotypic plasticity in teeth to extensively influence their diversity. Here, we review the literature concerning phenotypic plasticity of vertebrate teeth. Even though only a few taxonomically disparate studies have focused on phenotypic plasticity in teeth, there are a number of ways teeth can change their size, shape, or patterns of replacement as a response to the environment. Elucidating the underlying physiological, developmental, and genetic mechanisms that generate phenotypic plasticity can clarify its potential role in the evolution of dental phenotypes.

## Introduction

The primary function of teeth is to interact with the environment by procuring and processing food. Therefore, vertebrate dentitions are subject to strong environmental influences. However, the current dogma is that teeth are hard and immutable structures that solely dictate ecology but are rarely shaped by it. Nonetheless, the environment can have more profound effects on dental development than previously appreciated. To explore these possible impacts, we review the current literature focusing on phenotypic plasticity in vertebrate dentitions, that is, how environmental perturbations can affect tooth development (e.g., Kiliaridis 1986; Huyseune 1995; Nishimura et al. 2008; Wise and King 2008; Müller et al. 2014).

Because dentitions are constantly exposed to environmental influences, they could offer powerful phenotypes to study the importance of plasticity. Much is known about the biomechanics of teeth and their influence on feeding performance (Strait 1993; Lucas 2004; Strait et al. 2009; Ungar 2010; Santana et al. 2011; Becerra et al. 2013; Benazzi et al. 2013), but

knowing how the environment shapes these mechanical properties can provide additional insight into tooth function. Additionally, just as the morphology of teeth and food items shape feeding ecologies and foraging behaviors (Teaford et al. 2006; Vogel et al. 2009; Taniguchi 2015) the environment may affect the relationship between feeding success and fitness.

Tooth development and the genetic interactions contributing to dental morphology have most extensively been studied in mammals, but are generally conserved and well understood across vertebrates (Jernvall et al. 2000; Thesleff et al. 2001; Salazar-Ciudad and Jernvall 2002; Tucker and Sharpe 2004; Fraser et al. 2009; Smith et al. 2015; Hulsey et al. 2020a). However, during ontogeny, the environment also has ample opportunity to modulate tooth development. Human dentistry as well as disparate studies on some mammal and teleost species can provide insight into the ways in which the environment can shape dentitions, but it remains largely unclear what changes on the molecular level could be attributed to these environmental effects. Integrating function and

**Table 1** Studies explicitly reporting phenotypic plasticity in vertebrate dentition

Species	Environmental factor	Phenotype	Reference
<i>Astatoreochromis alluaudi</i>	Food hardness	Changes in tooth size	Huyseune (1995); Gunter et al. (2013); Schneider et al. (2014)
<i>Astatoreochromis alluaudi</i>	Food hardness	Changes in tooth number	Huyseune (1995)
<i>Oryctolagus cuniculus</i>	Food abrasiveness	Increased molar growth rate	Müller et al. (2014)
<i>Rattus rattus</i>	Food hardness	Anterior shift of incisor position	Kiliaridis (1986)
<i>Peromyscus maniculatus bairdii</i>	Food hardness	Anterior shift of incisor position	Myers et al. (1996)
<i>Archosargus Probatocephalus</i>	Food hardness	Increased enamel thickness	Worcester (2012)
Mouse	Orthodontic force	Changes in tooth position	Chen et al. (2016)
Mouse	Excision of primary teeth	Induction of tooth regeneration	Popa et al. (2019)
Human	Orthodontic force	Changes in tooth position	Wise and King (2008)
Human		Variation in first molar size	Dempsey and Townsend (2001)
Human	Mechanical force	Reparative dentinogenesis	Smith et al. (2003)
Human	Smoking	Delayed tooth eruption	Rantakallio and Mäkinen (1983)
Human	Malnourishment	Delayed tooth eruption	Garn and Rohmann (1966)
Human	Maternal age	Delayed tooth eruption	Wu et al. (2019)
Human	Physical-/psychological	Hypo-/hyperplasia of enamel growth lines	Guatelli-Steinberg (2001)

development into feeding ecology may elucidate how and why plastic tooth phenotypes have evolved and perhaps even how they become fixed.

A framework that integrates across biological disciplines should allow us to better understand how and when phenotypic plasticity can influence dental diversification (Ungar 1996; Lucas 2004; Tucker and Sharpe 2004; Fraser et al. 2006; Thesleff 2006; Fraser et al. 2013; Lucas et al. 2014; Popa et al. 2019). We first review the current literature about dental phenotypic plasticity as well as which environmental factors modulate these phenotypes (Tables 1 and 2; Fig. 1). We then discuss some developmental genetic mechanisms that are known to mediate plastic dental phenotypes. Finally, we discuss several scenarios that provide context for how and when phenotypic plasticity would be expected to play a role during the evolutionary diversification of teeth (Fig. 2).

## Axes of environmentally induced phenotypic changes in dentitions during ontogeny

### Tooth position

Teeth are exposed to a number of forces during mastication and prey capture that may impact their position on the vertebrate jaw. For instance, when rodents feed on hard food items, their incisors can shift anteriorly compared to individuals feeding on soft items (Kiliaridis 1986; Myers et al. 1996). The forces applied cause bone to be resorbed on the side

of the tooth where pressure is applied and new bone to be formed on the opposite side of the tooth (Reitan 1960; Wise and King 2008). This phenomenon of force causing teeth to move on the jaw, termed orthodontic tooth movement, has been used in dentistry for decades to correct dental mispositioning (Meikle 2005; Wise and King 2008). The importance of tooth movement as a plastic response to diet variability should be examined more extensively in a wider array of organisms because it could frequently affect the functional abilities of the dentition. For example, the location of teeth could determine the abilities of predators to capture and process prey, potentially allowing them to be more effective at resisting forces, piercing, or shredding food items (Mihalitsis and Bellwood 2019).

### Tooth growth rates

For some vertebrates, teeth erupt and do not grow following eruption. However, teeth do grow continuously in many mammals including walrus, elephants, mice, and rabbits, and continuous growth is often counteracted by tooth wear (Renvoisé and Michon 2014). Tooth wear, which is caused by almost all food items, is often induced by small mineral particles, either grit ingested when an organism feeds off the ground or silica crystals embedded within plant material (Metcalf and Chalk 1950; Fortelius 1985; Teaford 1988; Ball et al. 1993; Fox et al. 1996; Williams and Kay 2001; Lucas 2004;

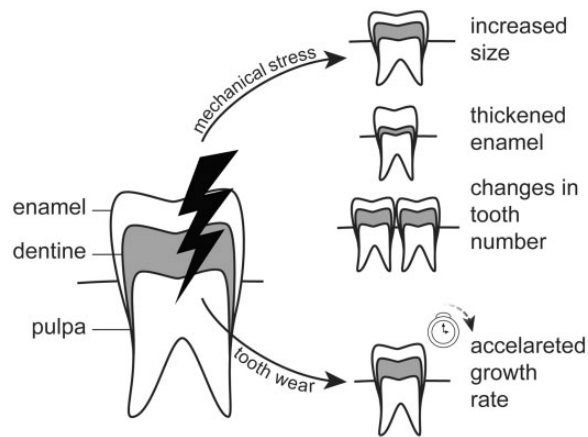
**Table 2** List of genes linked to phenotypic plasticity in vertebrate teeth, their identified function, and potential role during tooth morphogenesis

Gene	Function	Potential role during plasticity	Reference
<i>rgs2</i>	Regulation of G-protein signaling after mechanical stress	Sensing mechanical stimuli	de Araujo et al. (2007)
<i>ier2</i>	Immediate early response	Sensing mechanical stimuli	Schneider et al. (2014)
<i>cfos</i>	Transcription factor regulating osteoclast differentiation and involved in tooth eruption	Induction of osteoclast differentiation to promote eruption	Grigoriadis et al. (1994)
<i>alas1</i>	Haem biosynthesis	Increased deposition of iron to increase tooth hardness	Schneider et al. (2014)
<i>c1ql</i>	Haem gene	Increased deposition of iron to increase tooth hardness	Schneider et al. (2014)
<i>thbs3</i>	Adhesion molecule	Mediating cellular contact	Liu et al. (2011)
<i>col6</i>	Collagen matrix	Matrix scaffold for mineralization	Schneider et al. (2014)
<i>col12</i>	Collagen matrix	Matrix scaffold for mineralization	Schneider et al. (2014)
<i>runx2</i>	Regulating differentiation of odontoblasts and deposition of matrix genes	Increasing differentiation rates of odontoblasts during early odontogenesis and induction of matrix deposition	Chen et al. (2009)
<i>osx</i>	Regulating differentiation of odontoblasts during late stages of odontogenesis	Increasing differentiation rates of odontoblasts during late odontogenesis	Chen et al. (2009)
<i>des</i>	Intermediate filament expressed in dental pulp cells	Mediating cellular contact	Lombardi et al. (1992)
<i>tpm4</i>	Formation of enamel matrix patterns	Enamel patterning	Nishikawa et al. (1988)
<i>tnnt</i>	Muscle gene	Potentially involved in tooth movement	Schneider et al. (2014)
<i>anxa6</i>	Signal transduction in alveolar bone	Sensing mechanical stimuli	Salmon et al. (2013)
<i>ryr1</i>	Calcium channel	Regulation of tissue calcification	Barrey (2010)
<i>srl</i>	Regulation of calcium signaling	Regulation of tissue calcification	Schneider et al. (2014)
<i>abcb3</i>	Transmembrane transporter of the ABC-transporter family		Schneider et al. (2014)
<i>gif</i>	Vitamin B12 binding	Processing of dietary vitamin B12 to maintain dental function and counteract tooth loss	Zong et al. (2016)
<i>klf4</i>	Transcription factor regulating differentiation of dental pulp cells to odontoblasts	Increase in odontoblast differentiation	Lin et al. (2011)
<i>sox2</i>	Transcription factor important for maintenance of stem-cell niches in dental laminae	Increasing differentiation rates to promote tooth replacement	Popa et al. (2019)
miRNA-21	Micro RNA contributing to orthodontic tooth movement	Inhibition of tooth movement impairing genes (e.g., osteoprotegerin)	Chen et al. (2016)

Lucas et al. 2014). It has been shown that the emergence of continuously growing rabbit molars is accelerated when wear is more extensive (Fig. 1; Müller et al. 2014). For example, when grasses were supplemented with grit, molar growth rates increased: the more tooth volume was lost, the more tooth volume was replaced (Müller et al. 2014). It is unknown how widespread plasticity in growth rates is, but selection might be expected to commonly favor plastic responses to variability in tooth wear in organisms with continuously growing teeth.

### Replacement teeth: Shape and internal structure

While rabbits respond to dental attrition with increasing growth rates (Müller et al. 2014), other vertebrates could exhibit plasticity when replacing their teeth. Most vertebrates are polyphyodont, which means that they replace their teeth constantly throughout their lifetime (Cooper 1966; Lawson et al. 1971; Nakajima 1979; Kline and Cullum 1984; Kline and Cullum 1985; Smith and Coates 1998; Smith and Coates 2000; Fraser et al. 2009; Handrigan et al. 2010; Richman and Handrigan



**Fig. 1** Phenotypic plasticity in teeth: tooth phenotypes can change in response to the environment. With increasing food hardness, that is, higher mechanical force exerted on teeth, replacement tooth size increases, and tooth numbers change in cichlid fish (Huyseune 1995). The sheephead *Archosargus probatocephalus* develops teeth with increased enamel thickness as a response to high mechanical strain (Worcester 2012). When tooth wear increases, growth rates in rabbit molars increase to compensate for the lost tooth volume (Müller et al. 2014).

2011; Tucker and Fraser 2014). Many changes in replacement teeth are likely to reflect fixed differences, but these highlight how phenotypically distinct replacement teeth can be. For example, although they are diphyodont and only have one set of replacement teeth, human permanent dentition differs from the primary dentition in enamel thickness, tooth number, and shape (Nelson 2014). However, changes in shape and structure can be phenotypically plastic in other species. As an example, feeding induced mechanical forces have been found to affect replacement teeth in some fish species (Huyseune 1995; Worcester 2012; Hung et al. 2015). For instance, a positive correlation between tooth size in the crushing pharyngeal jaws and experimentally manipulated food hardness has been observed in the African cichlid *Astatoreochromis alluaudi* (Fig. 2A; Huyseune 1995; Gunter et al. 2013; Gunter and Meyer 2014; Schneider et al. 2014). In these fishes, the relative size of the replacement teeth increases in response to being fed hard food items (Fig. 2A). Tooth size in these fishes likely constitutes a trade-off. Although processing of soft plant-based food is generally more efficient with small and pointed teeth, greater tooth size is advantageous when crushing prey since larger teeth experience less strain at equal mechanical forces (Lucas 2004; He et al. 2013). To date, tooth size has only been shown to be phenotypically plastic in fish but could potentially play a role in the dentitions of other polyphyodont species like reptiles and some mammals (Huyseune 1995;

Gomes Rodrigues et al. 2011; Gunter et al. 2013; Hung et al. 2015).

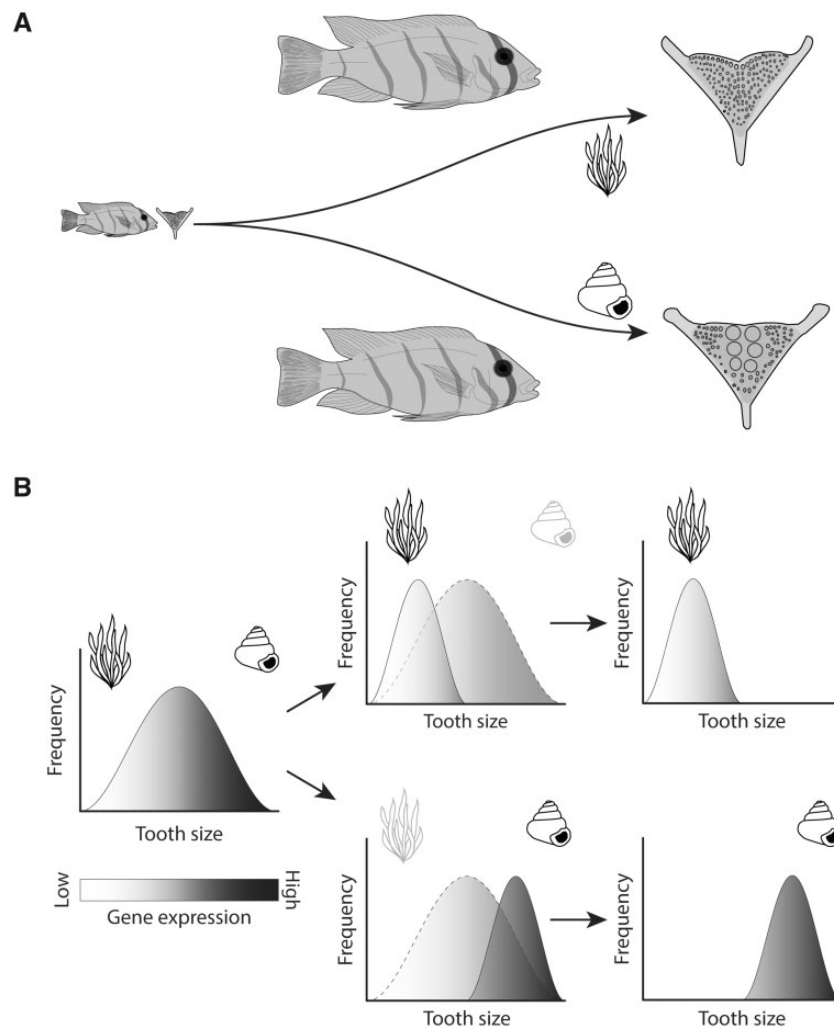
Another plastic response associated with replacement teeth that have been documented is the increase in enamel thickness as a function of food hardness (Worcester 2012). Enamel thickness plays an important role in determining what food items can be consumed, since it affects the fracture resistance of teeth (Dumont 1995; Lambert et al. 2004; Lucas 2004; Constantino et al. 2009; Santana et al. 2011). Phenotypic plasticity in enamel thickness can be observed in sheephead fish (*Archosargus probatocephalus*) where harder food items lead to an increase in the thickness of the enamel layer (Worcester 2012). The mechanisms behind this plastic response are unclear because enamel forming cells are shed after tooth eruption (Nanci 2017). In this species, it seems likely that replacement teeth, and not the erupted teeth themselves, develop thicker enamel layers. Given that the teeth of fish and many other vertebrates are frequently replaced throughout their lifetimes (Tuisku and Hildebrand 1994), there is a substantial opportunity for plasticity to influence phenotypes like tooth shape and internal structure in these polyphyodont species.

### Tooth numbers

Tooth numbers vary extensively between species and often evolve as adaptations to certain food items (Line 2003). However, intraspecific variation in tooth numbers can be readily observed (Eastman and Underhill 1973; Thorpe 1975; Greer 1991; Catzeflis et al. 2017) and some of this variation in many vertebrates might be phenotypically plastic. For instance, a decrease in tooth number has been reported for the African cichlid *A. alluaudi* following an extended period of feeding on hard food items (Huyseune 1995). However, tooth numbers are frequently inversely correlated with tooth sizes (Eastman 1977; Huyseune 1995; Strelman and Albertson 2006; Hulsey et al. 2020b). Whether a plastic decrease in tooth number in individuals consuming hard food items might stem from a limited dentigerous area and increased tooth size remains an open question. A decrease in tooth numbers in many vertebrates might also commonly be due simply to the non-adaptive loss of or damage to teeth that can occur when organisms feed on hard prey.

### Timing of tooth eruption

Although most mammals have only one or two generations of teeth, the timing of their tooth eruption and replacement can be strongly influenced by the environment (Garn and Rohmann 1966; Alvarez



**Fig. 2** Assimilation of tooth size (A) and underlying gene expression patterns (B) in cichlid fish: Hypothetical model of adaptation to hard food items in cichlid fishes. An increase in tooth size has been shown to be an adaptation to durable food items while smaller teeth can be found in species feeding on softer items like algae. (A) Initially, cichlid fish up to a certain standard length do not vary in tooth size. However, when fed different diets, as they grow, tooth phenotypes change. When fed on diets differing in hardness, *A. alluaudi* develop varying tooth sizes that are positively correlated with food hardness. (B) We hypothesize that fixed tooth size divergence between species is a product of genetic assimilation of the same developmental genetic mechanisms that is depicted by gene expression levels (shading of curves).

1995; Heinrich-Weltzien et al. 2013; Nicholas et al. 2018). Variation in the timing of human tooth eruption can arise frequently as a consequence of adverse conditions (Garn and Rohmann 1966; Heinrich-Weltzien et al. 2013; Ntani et al. 2015; Wu et al. 2019). Numerous studies have documented a delay in tooth eruption of malnourished children (e.g., Garn and Rohmann 1966; Alvarez 1995; Suri et al. 2004; Heinrich-Weltzien et al. 2013). Obesity, in contrast, speeds up tooth eruption (Nicholas et al. 2018). Psychological stress, maternal smoking habits, or premature birth also influences primary and secondary tooth eruption (Rantakallio and Mäkinen 1983; Guatelli-Steinberg 2001; Ntani et al. 2015; Wu et al. 2019). Additionally, although it is possible

that a plastic change in replacement tooth size or shape governs the documented response to harder food items in the African cichlid *A. alluaudi* (Fig. 2A; Huyseune 1995; Gunter et al. 2013; Schneider et al. 2014; Hung et al. 2015), there is a second possibility. Replacement of these crushing teeth could be accelerated. The relative size of pharyngeal replacement teeth later in ontogeny seems highly constrained across cichlids (Hulsey et al. 2020b), but if every generation of teeth is larger than the previous one, an increase in replacement rates would experimentally produce an increase in tooth size. Environmentally influenced changes in the timing of tooth eruption could play a role in dental variability in a large number of vertebrates



and the mechanisms governing this and other plastic responses should be more thoroughly investigated.

## Developmental genetics of dental plasticity

The documented repertoire of genes associated with changes in tooth position, tooth growth rates, and tooth replacement is constantly increasing (Table 2). Many conserved developmental genetic pathways of odontogenesis have been found to play a common role across virtually all major tooth-bearing vertebrate lineages (Tucker and Sharpe 2004; Vonk et al. 2008; Fraser et al. 2009; Jernvall and Thesleff 2012). Progress is now also being made to understand the molecular mechanisms behind environmentally induced changes in tooth phenotypes (Table 2; Papachristou et al. 2009; Yang et al. 2010; Mantila Roosa et al. 2011; Gunter et al. 2013). A deeper molecular understanding of dental plasticity could facilitate therapies to treat human dental pathologies as well as increase our knowledge about developmental genetic mechanisms governing dental diversity across all vertebrates.

Investigations of molecular mechanisms underlying phenotypic plasticity in teeth have already opened up potential gene therapies (Oshiro et al. 2002; Kanzaki et al. 2004; Kanzaki et al. 2006; Nishimura et al. 2008; Huang et al. 2014). For instance, orthodontic tooth movement can be accelerated via the application of mechanical stress (Nishimura et al. 2008). Rats treated with resonance vibration show an upregulation of *rankl* (receptor activator of nuclear factor  $\kappa$ B), a gene that is important for bone remodeling (Theoleyre et al. 2004; Nishimura et al. 2008). When administered into rat periodontal tissue via viral vectors, *rankl* significantly accelerates tooth movement (Kanzaki et al. 2006). However, the opposite effect is also possible: administration of the *rankl* antagonist *opg* (osteoprotegerin) inhibits tooth movement (Kanzaki et al. 2004). Tooth movement is also inhibited by a lack of microRNA-21 expression in rats (Chen et al. 2016). Such gene therapies could be developed for a multitude of pathologies or therapeutic measures if we understood the underlying genetic mechanisms that induce plasticity in dental phenotypes.

The molecular mechanisms underlying plastic responses outside of mammals have been most fully explored in the crushing pharyngeal dentitions of cichlids fishes (Gunter and Meyer 2014; Schneider et al. 2014). A set of candidate genes has been identified that may induce changes in tooth size in cichlid fishes when diet is changed. Gene expression

changes in the jaws of cichlids depending on if the fish are fed a soft or a hard diet (Gunter and Meyer 2014; Schneider et al. 2014). The interaction of two mechanisms has been proposed to explain how signals are conveyed from hard food items to the tooth-forming cells (Schneider et al. 2014). First, via G-protein mediated signaling, the cAMP-sensitive transcription factor *creb1* is activated. Activation of *creb1* leads to increased expression of bone matrix (e.g., *osx*) and calcium genes (e.g., *anxa6*) that are likely to play a role during jaw remodeling and tooth replacement (Schneider et al. 2014). Second, the strain sensitive transcription factor *ap1* reacts to hard food items affecting the expression of early-response genes (e.g., *cfos*) and collagens (e.g., *col6*), as well as calcium (e.g., *anxa6*) and muscle-related genes (e.g., *tpm4*; Table 2; Schneider et al. 2014). Both pathways, ultimately affect *runx2* expression, which plays an important role in differentiation of odontoblasts and for matrix deposition, so mechanically activating this gene can lead to more tooth-forming cells (Komori 2010; Han et al. 2014). Additional manipulative experiments are necessary to validate these proposed mechanisms. Also, there are likely a host of additional molecular mechanisms that influence dental plasticity in other vertebrates. However, the clarity of the environmental factors responsible for dental plasticity coupled with a more molecular understanding of underlying mechanisms can provide some of the clearest insight into how dental plasticity is initiated and even how plasticity could influence the evolution of tooth diversity.

## How might dental plasticity influence evolution?

The influence of plasticity on phenotypic evolution has long been questioned (West-Eberhard 1989; Via 1993; West-Eberhard 2003; Pigliucci et al. 2006; Lande 2009; Levis and Pfennig 2016), especially in seemingly inert traits like teeth (Gunter et al. 2017; Schneider and Meyer 2017). However, there are several hypotheses of how plasticity could contribute to adaptive evolution. For instance, the flexible stem model predicts that ancestrally plastic or “flexible” stem lineages represent the basal condition for many adaptive radiations (West-Eberhard 2003; Levis and Pfennig 2016; Schneider and Meyer 2017). Under this scenario, an initially plastic species has the potential to rapidly occupy multiple novel environments by first colonizing those environments and then producing the phenotype best suited to particular habitats with distinct resources (West-Eberhard 2003; Schneider and Meyer 2017).

Further, such plastic species are likely to be more successful at colonizing novel habitats than non-plastic species. Once novel and temporally stable habitats are colonized, selection can then act on the fixation of a subset of the previous phenotypic range and against phenotypic plasticity. Alternative phenotypes within the range of environmentally induced phenotypic variation that best match the new habitats could then become canalized in distinct populations of the original species (Bolnick et al. 2003; Muschick et al. 2011; Levis and Pfennig 2016; Gunter et al. 2017; Schneider and Meyer 2017). Selection on the phenotypes in the flexible stem lineages could also lead to genetic assimilation, that is, the expression of a previously environmentally induced phenotype without environmental influences (West-Eberhard 2003; Pigliucci et al. 2006; Lande 2009).

One system that offers great potential to test the possible role of phenotypic plasticity on adaptive evolution is cichlid fishes (Schneider and Meyer 2017). Focusing on cichlid pharyngeal tooth size to test the flexible stem model is advantageous for several reasons. Pharyngeal tooth size in cichlids is phenotypically plastic (Huysseune 1995; Gunter and Meyer 2014). Also, different tooth sizes have been fixed between closely related lineages multiple times independently across the cichlid phylogeny (Hulsey et al. 2008; Muschick et al. 2012; Karagic et al. 2020). Phenotypic plasticity in pharyngeal jaws is also reduced in derived species from the African adaptive radiations that inhabit more stable lake environments compared to lineages occupying the ancestral riverine environment (Gunter et al. 2017). Additionally, variation in expression of important genes is also reduced in derived lineages (Fig. 2; Schneider et al. 2014; Gunter et al. 2017). Therefore, evidence consistent with genetic assimilation already exists for the cichlid pharyngeal jaws (Gunter et al. 2017). However, as only a few candidate genes have been investigated in cichlids, the sequencing of whole transcriptomes will allow us to more extensively identify developmental genetic mechanisms that overlap between fixed and environmentally induced pharyngeal tooth sizes. Further studies could elucidate more finely the genes that are expressed in cichlids representing both the plastic as well as the putatively fixed lineages. Additionally, comparative examinations of flexible stem tooth phenotypes in other vertebrates would provide insight into the potential evolutionary importance and generality of this model to dental diversification.

A second scenario involving the crushing pharyngeal jaws of cichlids could also be envisioned whereby phenotypic plasticity might lead to adaptive divergence via the co-evolutionary escalation of pharyngeal tooth size with prey hardness (Fordyce 2006; Johnson et al. 2007; Chaves-Campos et al. 2011). Importantly, the coevolution of cichlids with their snail prey has been suggested to have occurred in several lineages (Chaves-Campos et al. 2011). If the cichlid fishes exhibited plasticity in their pharyngeal jaw for crushing snail prey, this may lead to strong selection for snails with harder shells (Fordyce 2006). Because snail generation time is much shorter than that of the fishes, the snails could rapidly evolve to have stronger shells. In order to exploit these harder snails, any plastic response that existed or arose would be advantageous. To keep pace with the ongoing selection for harder snails, mean tooth size would be expected to adapt along with any traits associated with crushing in the cichlid predator. In crushing predatory cichlids, adaptively plastic changes around the new adapted mean trait value could be induced so that the co-evolution with snail hardness is maintained. Under such a scenario, the evolutionary increase in shell hardness selected for by the plastic response in the predatory cichlids will feedback favoring the maintenance of phenotypic plasticity around a continuously increasing adapted mean (Eshel and Matessi 1998). This example remains hypothetical for cichlid fish dentition but provides an interesting possibility where maintenance of plasticity and continuous genetic assimilation could drive phenotypic evolution.

Dental plasticity may also have influenced the evolution of many other vertebrate lineages. Most mechanisms of dental plasticity discussed here can also be observed as fixed differences between closely related species. For instance, enamel thickness, which can be phenotypically plastic, can commonly be observed as fixed species differences in lineages like bats and primates (Dumont 1995; Lambert et al. 2004; Lucas et al. 2008; Santana et al. 2011). If we could isolate the genes that contribute to plastic dental phenotypes, in these and many other systems, we could determine if these same genes are fixed between closely related species that differ in the alternatively plastic phenotypes. Furthermore, if we could experimentally manipulate populations over time that vary in their plasticity as well as the plastically inducing characteristics of their prey, we could more robustly determine how and when plasticity contributes to the fixation of a diversity of dental phenotypes.

## Conclusions

Research on vertebrate dentitions encompasses a number of disparate disciplines (Lucas 1979; Thesleff and Hurmerinta 1981; Dumont 1995; Lucas 2004; Tucker and Sharpe 2004; Fraser et al. 2006; Fraser et al. 2009; Strait et al. 2009; Thesleff and Tummers 2009; Ungar 2010; Santana et al. 2011; Jernvall and Thesleff 2012; Hulsey et al. 2016). However, phenotypic plasticity has been largely ignored when studying vertebrate tooth diversity. To understand how the environment can shape dentitions and also play a role in evolutionary change, a more synthetic view is needed. This integration across dental disciplines will allow us to gain a more complete picture of how the environment interacts with the axes of variation in toothed organisms and exploits their developmental genetic machinery to produce phenotypic change in teeth.

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