EPIGENETIC ORTHODONTICS:

Developmental Mechanisms of Functional (Formational) Orthodontic Appliances

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9 months after DNA appliance
While there are several descriptions of functional orthodontic appliances, there is no official consensus on the definition of a functional orthodontic appliance. Moreover, there is a dearth of evidence on the developmental mechanism(s) by which functional orthodontic appliances achieve their effects. This article explores the concept of epigenetic orthodontics, which involves osteogenesis, a physiologic process of bone development during tooth correction. The molecular-morphologic basis of epigenetic orthodontics can be explained by the Spatial Matrix Hypothesis. Clinically, this hypothesis is implemented by foundational (skeleto-dental) correction using the DNA appliance™ system, with direct or indirect functional (myo-spatial) correction. These clinical protocols rely upon the natural process of sutural homeostasis, which is encoded by genes, and through which an enhanced level of craniofacial homeostasis can be achieved. This improvement includes not only better tooth alignment but also dentoalveolar bone development, as well as facial cosmesis, and optimization of the upper airway dorsal to the craniofacial complex. It is posited that epigenetic orthodontics encompasses the developmental mechanisms by which functional orthodontic appliances, perhaps better called formational appliances, achieve their clinical outcomes.

**Introduction**

Functional orthopedics is a term that has been used widely in the orthodontic literature. However, the definition of ‘functional orthopedics’ varies widely. Thus, it would be wise to examine the terminology associated with this discipline before proceeding to its detailed applications. In addition, many different ‘functional appliances’ are available e.g. Activators, Monoblocks, Twinblocks, Bioblocks, Bionators, Frankel’s etc. Therefore, one of the first questions to arise is: What is a functional appliance? According to the British Orthodontic Society (BOS), a functional appliance is a removable appliance that works on the upper and lower teeth at the same time. The BOS further states that functional appliances help correct skeletal problems, while the dental problems are corrected with fixed orthodontic appliances. This notion supports to the idea that foundational correction could proceed orthodontic correction with removable appliances such as aligners. But, other definitions of functional appliances can also be found. Some suggest that functional appliances are special removable appliances, which change the way the teeth and jaws bite together. Note that this definition varies from others they propose that functional appliances are removable or cemented appliances used to correct excess overjet problems. Yet others believe that functional appliances are a class of removable appliances that utilize the muscle action of the patient to produce orthodontic or orthopedic forces. Indeed, the British Dental Health Foundation suggests that it is sometimes possible to change the way the jaws grow, using functional appliances, and that these appliances use the power of jaw muscles to help with certain types of problems. Kalaf and Mattick also suggest that functional appliances are removable or fixed orthodontic appliances that use forces generated by the stretching of muscles, fascia and/or the periodontium to alter skeletal and dental relationships. Therefore, ostensibly, the effects of stretch during growth and development may be the mode through which functional appliances attain their treatment effects, and this idea has been extended to the use of aligners. Although this notion has been referred to as soft tissue stretch, results from permanently implanted electromyographic sensors demonstrated that lateral pterygoid muscle hyperactivity is not associated with functional appliances. Thus, other factors might play a more significant role in new bone formation.

The American Association of Orthodontists suggests that functional appliances are used to normalize growth discrepancies between the upper and lower jaw, and that removable orthopedic functional appliances can help correct growth discrepancies. Indeed, Gen suggests that functional appliances all have a similar purpose; to help jaws develop normally and achieve facial balance. According to the Canadian Orthodontic Association (COA) functional appliances can be used in growing patients to put the jaws in balance, achieve good facial muscle function and create natural facial proportions. However, the COA asserts that it is essential that orthodontic screening be done at 7 or 8 years of age to ensure that the patient is not too old for functional appliance therapy. However, data is now available that suggests that similar effects can be achieved in so-called ‘non-growing’ adults. The COA further suggests that these appliances can be designed to not only move teeth but also correct the alignment of the jaws, and that the most common objective is to correct an underdeveloped lower jaw. In a similar fashion, the Australian Society of Orthodontists (ASO) suggests that functional appliances are devices used to correct a significant disharmony in the relationship between the upper and lower jaws. The ASO further suggests that functional appliances work by influencing the growth and development of a growing patient. They suggest that
the most common use of a functional appliance is to encourage the forward growth of a retrusive or underdeveloped lower jaw. Indeed, functional appliances hold the lower jaw forward for a period of time until the teeth, jaws and joints have "adapted", and the desired jaw position has been obtained. Researchers at the University of Columbia, USA 13 also believe that a functional appliance is a device that alters a patient’s functional environment in an attempt to influence and permanently change the surrounding hard tissue. Therefore, it might be preferable to undertake a phase of foundational correction prior to the implementation of aligners in adults.

Ritto14 provides a classification of fixed functional appliances. Ritto14 proposes that functional orthopedics seeks to correct malocclusions, and harmonize the shape of the dental arch and oro-facial functions. Ritto14 further suggests that removable functional appliances are: large in size; have unstable fixation; cause discomfort; lack tactile sensibility; exert pressure on the mucosa (encouraging gingivitis); reduce space for the tongue; cause difficulties in deglutition and speech, and very often affect esthetic appearance. Ritto14 also suggests that the alteration in the mandibular posture creates difficulties, which make the adaptation and acceptance of functional appliances more difficult. Therefore, the potential deficiencies of functional appliances have been noted, and appear to include the age at which a patient can be treated, and a lack of precision in final tooth positioning inter alia, as noted above. These deficiencies could be addressed by using new appliances, such as the wireframe DNA appliance™15 that are more comfortable for the adult patient during the evenings and nighttime but are taken out during the day.

What is a Malocclusion?

Before prescribing an orthodontic appliance of any type, a diagnosis of malocclusion must be reached. Generally speaking, malocclusions are categorized according to Angle's classification i.e. Class I, Class II division 1 or division 2, and Class III. Interestingly, anterior open-bite is a form of malocclusion that is frequently seen clinically, but was never classified by Edward Hartley Angle. Why not? Before attempting to address that question, it would be wise to confirm the definition of a malocclusion. A cursory search on the world-wide-web reveals the following definitions for malocclusion:

- A condition in which the upper and lower teeth do not fit together properly
- Incorrect position of biting surfaces of the upper and lower teeth
- An inherited defect where the upper and lower jaws do not let teeth meet
- Improper alignment of the teeth
- A bad bite caused by incorrect positions of the upper and/or lower teeth
- Teeth that are misaligned or fit together poorly when the jaws are closed
- Malposition and imperfect contact of the mandibular and maxillary teeth
- Abnormal contact between upper and lower teeth
- A dental disease where the teeth overgrow
- An abnormal alignment of the teeth
- Disharmony in the way upper and lower teeth come together when biting
- Abnormal or malposition relationships of maxillary to mandibular teeth
- Abnormal occlusion of the teeth or jaws
- A bad bite, which includes crowded or crooked teeth or misaligned jaws
- A condition in which the opposing teeth do not mesh normally

Therefore, there are several descriptions of malocclusion, but there is no official consensus on the definition of a malocclusion. Indeed, none of the above definitions indicates the underlying etiology of malocclusions. Therefore, Singh16 defined a malocclusion as a solution for a complex, adaptive system to remain in equilibrium. The complexity referred to in the above definition is twofold. First, structural complexity is built in the craniofacial system, which comprises teeth, bone, muscles, joints, soft tissues and functional spaces. Second, mathematical complexity is in-built in the craniofacial system - due to any permutation or combination of genes being inherited and expressed, according to the functional genomics of the individual patient. Thus, a given malocclusion is a stable condition, being arrived at through developmental compensation. The crowns of teeth are unique, however, in that once their enamel is fully formed there is no developmental mechanism to change their size or shape. Tooth morphology can change minutely over a period of time, however, through attrition, abrasion and erosion or more quickly through invasive dental interventions, such as inter-proximal reduction or slenderizing. Nevertheless, because of the unyielding properties of enamel, the crowns of teeth take up the space made available to them during the course of development i.e. eruption, and if this space is insufficient in any of the three
dimensions then a malocclusion arises. Normally, due to temporospatial patterning, and given appropriate gene-environmental interactions, teeth will align themselves following the curves of Monson and Spee because of tooth morphology, which has evolved over millennia, to produce a Class I occlusion. In modern societies, however, altered gene-environmental interactions (e.g. bottle-feeding, digit-sucking etc.) mean that teeth can end up in positions in which they are not optimal in terms of either function or esthetics. Thus, foundational correction could place the teeth close to their optimal functional position while aligners could be used to detail the final esthetics.

In addition to complexity, however, the craniofacial system has adaptability. The framework of the jaws is built from bone which, due to its rich vascularity, has a high degree of plasticity. This means that the facial skeleton can undergo bone remodeling in response to functional stimuli. Thus, while the teeth are actively erupting, their roots and supporting bone are subject to functional stimuli, which mold the final outcome. For example, if an object (such as a pacifier, soother or dummy) is placed close to the eruptive pathway, the teeth are in effect deflected into a position different than that determined by temporospatial patterning alone. However, the teeth retain their pre-determined morphology while the enclosing bone is ‘deformed’ through remodeling. This means that the application of an appropriate signal that remodels the bone can result in the correct re-positioning of the teeth. Thus, both bone morphology and tooth position need to be addressed.

Despite the propensity for adaptability, the final arbitrator is stability. The craniofacial system needs to be in balance or equilibrium in accord with functional demands; for example sufficient space for the tongue during sleep, speech, swallowing and mastication. Thus, a developmental compromise may be reached with the teeth in a less than ideal position but in a state in which a state of craniofacial homeostasis has been reached. According to the Spatial Matrix Hypothesis\textsuperscript{17}, during growth and development the craniofacial system adapts through developmental compensation until a new position of functional stability has been reached. Moreover, fixed and functional orthodontic appliances may modulate this state of developmental stability to the benefit (or detriment) of individual patients. Therefore, it is important to aim for improved craniofacial homeostasis and not improved tooth position alone.

**Spatial Matrix Hypothesis**

In the recent debate on the etiology and management of malocclusions, it has been noted that malocclusions are commonly encountered in modern civilizations, most likely due to changes in environmental conditions, such as feeding behavior. Thus, malocclusions might begin at birth, as modern mothers are less likely to breastfeed a child, whereas primitive cultures did so exclusively. Similarly, while the young children of primitive cultures did not ever use pacifiers nor were ever bottle-fed, these recent changes in environment/behavior might be associated with malocclusions such as anterior open-bite, which was so rare even a century ago that Angle omitted this malocclusion from his classification system. Indeed, recent work by Corruccini et al.\textsuperscript{18} points to canalization. Put simply, the amount of genetic variance is suppressed or buffered by (canalizing) environmental factors to produce certain outcomes, such as Class I, Class II and Class III malocclusions. But, when the environmental influences changed, the
amount of genetic variance increased, producing 'new' types of malocclusions that are modulated by environmental influences in the new, urbanized condition. Thus, anterior open-bite, unilateral posterior open-bite, vertical maxillary excess ('gummy smile'), etc. may be regarded as relatively 'new' developmental compensations produced by genetic variance and environmental interactions. In addition, however, there is no doubt that there is a certain genetic susceptibility to developing a malocclusion, as genes that encode for skeletal, muscular and dental tissues have been identified and sequenced. The famous Hapsburg's jaw is one example of this familial tendency for the development of a malocclusion. Familial hypodontia (oligodontia) is another example. Therefore, bone remodeling should be an integral part of treatment planning prior to the deployment of aligners.

Generally speaking, a cranio-caudal gradient of development exists in the human embryo i.e. structures in the head region appear first and undergo development prior to those located further distally. Thus, an altered maxilla, due to temporo-spatial patterning and gene-environmental interactions, has concomitant effects on the developing mandible; and these effects can sometimes be clearly seen in children who manifest a malocclusion as part of a craniofacial syndrome. In order to explain these associated phenomena the Spatial Matrix Hypothesis was developed using the Functional Matrix hypothesis as a starting point, which according to Moss was first formulated by van der Klaauw. As noted above, the crowns of teeth are unique in the human body because once fully developed there is no innate developmental mechanism by which they can change their size or shape unless subjected to interproximal reduction or slenderizing. They can, however, change their spatial position/orientation secondary to other tissues that are capable of: remodeling, such as bone; hypertrophy/atrophy, such as muscle; or regeneration, such as epithelia and the periodontium. Using this concept as a premise, it is likely that an underdeveloped midface presenting with palatal insufficiency (due to gene-environmental interactions) could be associated with malocclusions, and may simultaneously predispose to temporo-mandibular joint dysfunction (TMD) and upper airway compromise, such as obstructive sleep apnea (OSA). Indeed, preliminary findings suggest that a relationship may exist between TMD and upper airway morphology, as well as OSA and (nocturnal) bruxism. These findings interface well with the Spatial Matrix Hypothesis; a lack of functional space (to breathe at night) might set off an anxiety response that manifests with a patient grinding the teeth in an ineffectual, subconscious attempt to alleviate the airway. Indeed, it can be surmised that the existence of wear facets on permanent deciduous teeth is indicative of latent airway issues. Although currently there is a dearth of evidence for this notion, preliminary findings support the above contention that midfacial development is associated with airway improvements in adults. However, according to the Spatial Matrix Hypothesis, in the presence of developmental compensation, retraction/extraction and IPR/slimmering procedures during orthodontic treatment or inappropriate ‘prophylactic’ occlusal equilibration protocols may exacerbate a precarious state of developmental stability. Thus, in order to re-establish or enhance craniofacial homeostasis, special attention must be given to non-mandibular constraints in patients who present with a retrusive mandible, OSA or TMD. In other words, the cranioaxillary structures might need to be more thoroughly assessed before planning the final positions of the crowns of teeth.

**Form and Function**

The concept that ‘Form follows Function’ is replete in the medical and dental literature. If that premise is true then, conversely, the notion that ‘Deformity follows Dysfunction’ is also true. It has been suggested that functional appliances somehow alter function, yet there is a dearth of evidence to support this notion. Nevertheless, it is likely that functional alterations occur secondarily to the implementation of functional appliances, and the primary mode of correction may reside elsewhere in the craniofacial system. For example, when a functional appliance is used to re-position a retrusive mandible, there is a functional change in the upper airway. This mandibular advancement usually changes/improves the caliber of the upper airway and thereby improves airway function, according to Poiseuille’s equation - but the mechanism of correction of the malocclusion is not dependent upon the change in airway function. It was thought that by changing the position of the mandible, muscles or soft tissues were stretched, and that this stretch produces forces that somehow correct the malocclusion. This is but partly true. Recent evidence suggests that by changing the spatial relations of the mandible, a change in the pattern of gene expression is induced. **“Recent evidence suggests that by changing the spatial relations of the mandible, a change in the pattern of gene expression is induced.”**
of the overall correction required to resolve the malocclusion. In other words, a ‘functional’ mandibular appliance most likely induces a change in Form (of the mandible) primarily, and not its function primarily. Therefore, functional appliances may be better referred to as “Formational” appliances. These Formational appliances address the issue of deformity primarily and dysfunction secondarily, in line with the notion of form and function.

Similarly, when ‘functional appliances’ are worn, they often change/deteriorate the quality of speech. This change in function is detrimental and can be described as dysfunctional. The change occurs as the functional appliance encroaches on the tongue space inter alia. It is now known that a minimum speaking distance exists for each individual patient. Nevertheless, it is likely that this dysfunctional alteration is a secondary effect in the implementation of Formational appliances, and the primary mode of correction of the malocclusion must reside elsewhere in the craniofacial system. According to the Spatial Matrix Hypothesis, this change in jaw (and tongue) relations provides the impetus for a skeletal (foundational) correction, which addresses the jaw deformity, and is reliant upon an altered pattern of gene expression. Fortunately, the DNA appliance system is designed to be worn during the evenings and nighttime so that interference with speech is not an issue. In addition, when functional appliances are worn, there is a change in masticatory function. Yet, the teeth are not in contact during mastication – so how was the malocclusion unravelled, with the teeth showing good interdigitation at the end of functional appliance treatment? It was thought that by changing the pattern of mastication, muscles or soft tissues were stretched, and that this stretch produced forces that somehow corrected the malocclusion. This stretch response may be implicated in the correction of the malocclusion, leading to bone formation, for example. Indeed, stretch-sensitive genes have been identified in the mammalian genome. Nevertheless, the DNA appliance system has been designed to be not worn during eating so interference with mastication is not an issue. Thus, functional appliances might be better referred to as Formational appliances, which harness the developmental mechanisms of osteogenesis (endochondral and intramembranous ossification).

Another class of functional appliances can be grouped together under the generic name of “Palatal expanders”. Palatal expansion is another incompletely understood protocol that is used with large amounts of clinical success in functional orthopedics. Is there some unknown link between mandibular re-positioning and palatal expansion? In other words, is there a common maxillo-mandibular developmental mechanism that the craniofacial system can utilize to correct a malocclusion? The answer appears to be definitive in the evidence-based dental and orthodontic literature. Molecular biologists have found, over the past few decades or so, the physiologic process of Signal Transduction. This process occurs at the cellular level whereby certain cytochemical signals or cytokines are produced. These cytochemical signals or cytokines are often referred to as ‘growth factors’ simply because they were first iden-
tified in embryos. (These growth factors often have effects other than growth and development alone.) Nevertheless, when a specific growth factor, such as Bone Morphogenetic Protein (BMP) attaches to its specific Receptor on the cell surface, signal transduction occurs and produces a second messenger inside the cell’s cytoplasm. This second messenger effect is often associated with a rise in the level of cAMP in the cell. Within the cell cytoplasm, a cascade of events is initiated. Molecules that are activated in the cytoplasm translocate into the cell’s nucleus. Here they form complexes with nuclear co-factors. These complexes modulate i.e. up-regulate or down-regulate the pattern of gene expression. For example, if a gene is up-regulated, it is transcribed. This gene transcription leads to the biosynthesis of mRNA. The mRNA is detectable in the cell cytoplasm, and so the level of gene expression can be monitored using modern techniques of molecular genetics such as PCR (Polymerase Chain Reaction, which is a technique for copying and amplifying complementary strands of a target DNA). Indeed, PCR is dependent on a RT (Reverse Transcriptase; an enzyme that makes a DNA copy of a segment of single-stranded RNA). Moreover, the mRNA leads to the biosynthesis of specific proteins; for example, those involved in bone formation (osteogenesis).

The question now becomes: How do functional (Formational) appliances harness the physiologic mechanism of signal transduction? The answer is a specific form of signal transduction called Mechanotransduction. In this case the signal that the cell receives is not a cytochemical molecule but a mechanical or physical signal, such as stretch, deformation or a change in proprioceptive information. This change can be induced using the DNA appliance system or aligners etc. For example, when teeth meet in occlusion a certain amount of proprioceptive information is exchanged, which keeps the teeth in a stable occlusal relationship. If an opposing tooth is extracted, the proprioceptive information changes, and the change in spatial relations is detected by mechanoreceptors in the periodontium and periosteal membranes. This change in spatial relations produces signal transduction, which ultimately leads to a change in the pattern of gene expression, mRNA biosynthesis etc., until a new position of stability is eventually reached (Fig. 1).

This example succinctly encapsulates the central core of the Spatial Matrix Hypothesis. Moreover, changes in spatial relations induced when wearing functional (formational) appliances stretch or compress soft and hard tissues of the craniofacial system. These changes are detected by mechanoreceptors in the periodontium and periosteal membranes, and the ensuing developmental events can be harnessed for the correction of the malocclusion through the biosynthesis of new tissues, such as bone formation i.e. osteogenesis. Therefore, functional appliances might be better referred to as Formational appliances. But, how can this biologic phenomenon be controlled?

Sutural Homeostasis
During growth, the spatial and functional alignment of skeletal elements is maintained through remodeling of bony surfaces, including the periodontium, to permit function. For example, in a young child as the brain grows the calvaria are spread apart, and bone is deposited and remodeled to provide a protective covering for the expanding brain. But, environmentally-induced changes in the early morphologic relationship can produce a new solution or outcome. For example, native head-binding was practiced in certain South American cultures. The calvaria of these individuals appear deformed or abnormal compared to the normal skull morphology of that ethnicity, even though there was no functional deficit. Thus, departure from a genetically encoded ‘developmental program’ leads to identifiable abnormalities, which may or may not show dysfunction. For example, deformational (positional) plagioccephaly is relatively common in some modern cultures.

While the etiology of deformational/positional plagioccephaly is incompletely understood, changes in child-rearing practices may play a role. For example, laying the baby on a flat surface or in a child car-seat for prolonged periods may deform the calvaria, precipitating deformational/positional plagioccephaly. Applying this principle to structures caudal to the cranium, temporomandibular joint dysfunction (TMD) may affect the jaw joints, malocclusions may affect the dentition, and obstructive sleep apnea (OSA) may affect the upper airway, etc. In each of these examples, developmental compensation occurs to permit compromised function, in accord with the Spatial Matrix Hypothesis. Therefore, a necessary first step in the treatment of TMD, malocclusions and OSA is decompensation. In other words, appropriate spatial signaling can re-establish (genomic) pattern formation for optimal form and function. This change is spatial relations can be achieved by using functional (Formational) appliances such as the DNA appliance system prior to introducing aligners.

Recent work on suture biology has elucidated the developmental mechanisms by which the above corrections might be achieved. First, it is important to understand that human sutures do not synostose even in adults27 as previously thought. Second, a suture is a joint formed between two bones that undergo intramembranous ossification. In the embryo, sites of signal transduction indicate locations where bone formation occurs de novo. These sites are often referred to as ‘ossification centers’. The ossification radiates outwards and eventually two skeletal elements come into close approximation, for example as cranial sutures. It is now thought that sutures are subject to sutural homeostasis. Kambara28 suggested that intermittent forces could: open a suture; stretch sutural connective tissues; induce new bone deposition, and be subject to homeostasis, which maintained the suture width. Put simply,
if the suture separating two bony elements is less than 250μm in width approximately, bone will be resorbed until the sutural width is restored. Similarly, if the sutural width is greater than about 250μm, bone will be deposited until the sutural width is maintained. The actual sutural width varies and is about 100-400μm at any one time. Note also that separation of cranial sutures by an expanding brain volume is associated with bone deposition. Thus, the notion of stretch or tension is implied in osteogenesis.

It is interesting to note that the periodontal space on a periapical radiograph of a healthy tooth is usually around 0.25mm in width. As well, historically-speaking, in palatal expansion appliances the midline screw is turned by about 0.25mm. Clinically, it has been found that this amount of activation appears to work reasonably well in most cases. Perhaps it is a coincidence that 0.25mm = 250μm? Be that as it may, it is posited here that the periodontium behaves like a ‘periodontal suture’. In other words, the periodontium does not behave like a passive periodontal ‘ligament’ but as an active site subject to sutural homeostasis. Thus, during orthodontic manipulation of a tooth, the periodontal suture will actively deposit or resorb bone to maintain the periodontal space at approx. 250μm. Note that the periodontium is rather unique in the adult human as it appears to maintain fetal-like behavior. The human periodontium is a highly vascular tissue, unlike other ligaments, and has a high rate of turnover, similar to fetal tissues. Indeed, it is posited here that if the periodontium was to undergo maturation this would result in ankylosis of the teeth. For example, in certain instances, especially in the deciduous dentition, ‘submerged’ or ankylosed teeth can be found – and this feature may be characteristic in certain parents and their offspring, suggesting a familial tendency. But how can the developmental mechanism of sutural homeostasis be utilized clinically?

**Foundational Correction**

As alluded to above, malocclusions represent developmental compensation, and so a necessary first step in the correction of a malocclusion is decompensation using, say, the DNA appliance system. This decompensation is directed towards the skeletal components because bone was likely deformed during the formation of the malocclusion. This skeletal correction involves the formation and remodeling of new bone. Therefore, osteogenesis needs to be invoked, and this is achieved by: changing the maxillomandibular spatial relations; providing ultra-light mechanical signals (e.g. stretch) to induce gene transcription, and then guiding the teeth into good interdigitation using aligners for the dental correction. This procedure succinctly encompasses the notion of Foundational (skeletal-dental) correction. In other words, Formational appliances are unlikely to rely on forces to correct tooth position. As long as the tooth has sufficient space (i.e. bone volume) by the use of a Formational appliance, and is given appropriate signals, it can be guided into place using aligners. So if functional appliances are in reality Formational appliances, what is functional correction?
Functional Correction

Functional correction occurs either indirectly or sometimes directly in association with Foundational correction (Fig. 2), as described above. It is posited here that by providing developmental decompensation of the maxilla (e.g. through a DNA appliance procedure, which is a foundational correction based on the formation of bone) the spatial matrix is changed to one that aligns more closely with the temporospatial pattern encoded at the genetic level. This change in maxillo-mandibular spatial relations then permits optimal mandibular development, in accord with the genome of the particular patient (Fig. 3). In certain cases, orthodontic clinicians will report ‘spontaneous correction’ of the mandible, for example (Fig. 4).

Note that due to heterogeneity, not all patients are able to respond in this way. In other words, additional gene-environmental interactions are required for these patients. Thus, functional corrections, allied with the foundational corrections described above, may produce stable results in terms of both function and esthetics. These clinical protocols rely upon the natural process of sutural homeostasis, through which an enhanced level of craniofacial homeostasis can be achieved (Fig. 5).
Conclusions

- Functional appliances may be an historical misnomer, and these types of appliance may be preferentially referred to as Formational Appliances.

- Formational Appliances rely upon epigenetic orthodontics, which is a physiologic process that involves bone development during tooth correction.

- The molecular-morphologic basis of epigenetic orthodontics can be explained by the Spatial Matrix Hypothesis.

- Clinically, this protocol is implemented by Foundational (skeletal-dental) correction with direct or indirect Functional (myo-spatial) correction.

- These clinical protocols rely upon the natural process of sutural homeostasis, which is encoded by genes, and through which an enhanced level of craniofacial homeostasis can be achieved.

References

1. British Orthodontic Society Home Page www.bos.org.uk
2. www.joemitchellothodontics.com/treatment/dictionary.html
3. www.braces.org/healthcareprofessionals/dentists/glossary/c/fm
4. British Dental Health Foundation Home Page www.dentalhealth.org.uk
5. Kalaf and Mattick, University of Newcastle upon Tyne, UK
10. Canadian Association of Orthodontists Homepage www.caao-aco.org
13. Mascia VE. Columbia University USA

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