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Vienna - Chicago:

The cultural transformation of the model system of the un-opposed molar

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Abstract

The discussion over the roles of genes and environment on the phenotypical specification of organisms has held a central role in science philosophy since the late 19th century and has re-emerged in today's debate over genetic determinism and developmental plasticity. In fin-de-siecle Vienna, this debate coincided with a philosophical debate over empiricism/materialism versus idealism/ vitalism. Turn-of-the-century Vienna's highly interdisciplinary environment was also the birthplace for the model system of the unopposed molar. The un-opposed molar system features new tissue formation at the roots of teeth and tooth drift once opposing teeth are lost. The un-opposed molar model system was revived by a group of Viennese scientists that left Vienna during the Nazi period to address Vienna's questions about evolution and heredity and about genes and environment in Chicago's post-WWII scientific exile community. Here we are using the colorful history of the un-opposed molar to investigate the role of culture and method in the scientific evolution of a model system.

Introduction - From Clinical Observation to Philosophy of Nature

Vienna's fin-de-siecle (1890–1914) has been one of the quintessential periods in Western history of the mind, characterized by intense philosophical debates and dramatic societal changes. Few other European cities have been torn as much by the opposites of new and old, Socialists and Nationalists, and of Belle Époque and Modernism. Rarely has philosophy of nature played such a central role in the intellectual life of a city as in Vienna's debate between 19th century idealism and 20th century realism, between vitalism and reductionism, and between Neo-Darwinism and Neo-Lamarckism. And it is difficult to imagine a city that has thrived as much on the dialogue between these apparent dichotomies as Vienna, with its hundreds of coffeehouses and thousands of intellectual circles and discussion groups. This sparkling intellectual environment was also the cradle for the birth of a new discipline entitled "Oral Biology" dedicated toward the pathology, anatomy, histology, and physiology of the oral cavity. The intellectual fathers of this new Vienna School of Oral Biology were a group of Jewish clinician scientists around Bernhard Gottlieb (1886–1950), including Balint Orban (1899–1960), Rudolf Kronfeld (1901–1940), Harry Sicher (1889–1974), and Joseph-Peter Weinmann (1896–1960).

For Vienna's Oral Biologists, and especially for Weinmann and Sicher, the study of the design of the skull and the teeth was just one aspect of understanding fundamental philosophical questions about the design and the growth of organisms. Sicher and Weinmann's interest was in the role of genes and environment as they impact morphogenesis of the skeleton and about the continuous growth of the skeleton. For Sicher, the continuous eruption of teeth throughout life and the biological model of tooth movement through resorption and apposition were part of an orthogenetic "form follows function" approach toward skeletogenesis. Moreover, the phenomenon of opposing directions of tooth drift in rodents and mammals indicated that "genes" in an orthogenetic sense were transmitting different inherited information in different orders of animals. While dated today, the basic issues of Vienna's orthogenesis discussion

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about the role of genes and environment in the generation of phenotypes has found a recent revival in the debate over genetic determinism and developmental plasticity.

In their World War II exile Chicago, Sicher and Weinmann revived one of the model systems from Vienna times: the model of the un-opposed molar. The un-opposed molar model is a perfect example for the continuous axial and horizontal movement of teeth through continuous periodontal tissue remodeling. For Weinmann and Sicher's Chicago years (1938~1960), the questions about skeletal growth and remodeling as they are exemplified in the un-opposed molar phenomenon became an intellectual homage to Vienna's philosophical questions about the growth and design of organisms. In the present article, we will follow the intellectual journey of the un-opposed molar model from a simple clinical observation surrounded by a turbulent philosophical environment to its transformation into a vehicle for science philosophical questions in the émigré environment of Chicago's dental schools.

Naturphilosophie and Empiricism in fin-de-siecle Vienna

Vitalism versus empiricism

19th century science philosophy in Vienna centered on questions of heredity and empiricism and their interpretation in relationship to classic authorities such as Kant and Aristotle (Fig. 1). Throughout 19th century romanticism, and in part as a result of often mis-guided interpretations of Kant's critical theory, German Naturphilosophie gave birth to a number of theoretical concepts in order to explain non-reductionist aspects of our physical world that might correlate with Aristoteles' entelechia or with a higher meaning of life, including Jacob von Uexkull's Planmasigkeit, Hans Driesch's Psychoid, Johannes Müller's vitalism, which was favored by Harry Sicher (one of the Vienna Oral Biologists). Late 19th century neo-vitalism and Naturphilosophie were heavily opposed by Vienna's pre-eminent physiologist Ernst Wilhelm von Brücke. Together with Hermann von Helmholtz in Berlin, Brücke was one of the first to propose that all vital manifestations of an organism were the result of physical-chemical forces (reductionism, mechanicism). Brücke found support in Vienna's chairs in philosophy, who favored reductionist-empiricist approaches. Vienna's empiricist school of philosophy started with Franz Brentano, who introduced the concept of an empirical philosophy, followed by the physicist-philosophers Ernst Mach and Ludwig Boltzmann, and reached its culmination with the Vienna circle, whose members Rudolf Carnap and Moritz Schlick accepted as scientific judgments only those that could be verified by experiments.

Darwinism versus neo-Lamarckism

Darwin was introduced to the University of Vienna through the teachings of the comparative anatomist Karl Brühl (1820–1899), the zoologist Carl Friedrich Claus (1835–1899), and the physiologist Ernst Wilhelm Brucke (1819–1892). As a reaction to Darwin's theory of evolution, neo-Lamarckism evolved as an attack on Darwin's concept of natural selection as the primary factor in evolution, emphasizing the importance of environmental factors in phenotypic changes and retaining the concept of inheritance of acquired characters. Among the neo-Lamarckian concepts was the Orthogenesis theory as evolution by definitively directed variation as it was developed by Theodor Eimer, Henri Bergson, and Pierre Teilhard de Chardin. In Vienna, the idea that acquired habits may be transmitted to descendents was shared and propagated by many of Vienna's most eminent physiologists and zoologists, among them Karl Ewald Konstantin Hering (1834–1918), Richard Semon (1859–1918), and Sigmund Exner (1846–1926), who lectured and published extensively on the topic of "Memory as a Universal Function of Organized Matter" (mnetic engram hypothesis). The neo-Lamarckian concept of inheritance of acquired characters found its most prominent advocate in Paul Kammerer, whose experiments on the Lamarckian inheritance of nuptial pads in midwife toads have later been labeled fraudulent. Paul Kammerer was a member of the Vivarium, a circle of

Jewish experimental biologists that included among others Karl Przibram, Leopold von Portheim, Wilhelm Figdor, Eugen Steinach, and the young Julius Tandler who was to become the academic mentor of the Vienna Oral Biologists.

Naturphilosophie and the Vienna School of Oral Biology

Neo-Lamarckian influences

Both the Neo-Lamarckian theories of the Vivarium and the mnetic engram concept of the Hering-Semon-Exner school influenced the Vienna School of Oral Biology. Harry Sicher's teacher Julius Tandler (1869–1936) was inspired by Eugen Steinach's work on rejuvenating glands and conducted a research expedition to the woods of Bosnia to search for miraculous noble deers who were believed to carry rejuvenating properties. In his own publications, Sicher revealed himself as a close follower of Hering's and Semon's mnetic theory (1–5). Side-by-side with Neo-Lamarckism, Sicher endorsed Darwin's theory of favorable variation, especially in relationship to the genesis of rudiments (4), which he believed to support the "form follows function" approaches of the Viennese functional anatomy tradition. Sicher's mentor Julius Tandler was famous for constantly relating anatomical form and physiological function in his teachings and publications (6). Sicher himself was the last in this legendary tradition of Viennese functional anatomists, openly admitting that he was unable to think of structure being divorced from function (7). Weinmann and Sicher were repeatedly paying tribute to this tradition when they dedicated chapters of "Bone and Bones" to the topic of "Functional Adaptation of Bones" and "Adaptational Deformities of the Skeleton". Even in their analysis of tooth movement, they understood bone apposition and resorption as an expression of proper anatomical and functional position (8).

Orthogenesis, genetic determinism, and developmental plasticity

Early 20th century Vienna orthogenesis debate has found a modern counterpart in the current discussion over genetic determinism and developmental plasticity. Genetic determinism proposes that physical and behavioral phenotypes are largely determined by genes while developmental plasticity implies that phenotypes are not "random" variants, because their initialform reflects adaptive responses with an evolutionary history (9). The concept of developmental plasticity also suggests that genes are secondary factors in evolutionary change because environmentally initiated noveltiesmay have greater evolutionary potential than mutationally inducedones (9). This debate over the influence of genes and environment on phenotypes clearly invokes Vienna's debate over the role of hereditary and environmental factors in the design of the skeleton. And while Sicher's orthogenesis concept appears dated in the light of contemporary evolutionary biology, its modern counterpart of a reorganization of an ancestral phenotype followed by genetic accommodation (9) is not.

Biological Mechanisms Involved in the Maintenance of Occlusal Balance and Tooth Eruption

As mentioned above, the primary model system that the Harry Sicher and Joseph-Peter Weinmann used to verify their philosophical concepts was the model system of the un-opposed molar. This model system mimics a clinical situation in which antagonistic teeth from the opposing jaw have been removed, resulting in a super-eruption of the remaining teeth. The process that balances teeth from both jaws as long as teeth from both opposing jaws are present is called dental occlusion. Dental occlusion is defined as the physical contact of the biting surfaces of opposing teeth or their replacements and involves the coordinated functional interaction between the various cell populations forming the masticatory system as they differentiate, model, remodel, fail, and repair (10). In respect to individual teeth, physiological occlusion is maintained by a balance of forces from the upper and lower jaw which are transduced toward the periodontal apparatus and affect the equilibrium of mechanotransducing signals in the periodontium. Once teeth are no longer in an occlusal status, e.g. after the removal of an opposing tooth, this equilibrium of forces is out of balance and a new set of mechanosignals is transmitted to the tooth root, the periodontal ligament, and the alveolar bone. Together, stimulatory (RANKL, M-CSF) and inhibitory (OPG) factors form a balance in the regulation of deposition (11) and bone resorption (12), and off-setting this balance might be one of the key factors in the initiation of periodontal remodeling as it relates to vertical tooth movement. In the un-opposed molar model, the loss of antagonists resulted in super-eruption lower molars by means of new cementum and alveolar bone apposition as well as distal tooth migration by mesial alveolar bone apposition and distal bone resorption (13–15)(Figs. 3,4). This apposition of new cementum and alveolar bone is associated with defined changes in the network of extracellular matrix related growth factors, signals and gene products, including FGF9, collagen I, elastin, and proteoglycans (14–15).

The original biological system that served as a template for the experimental rodent model of the un-opposed molar was based on a typical clinical situation in patients following tooth extraction: the tipping, supra-eruption, and drift of neighboring teeth. The model system was born in Bernhard Gottlieb's oral histo-pathological laboratory in pre-WWII Vienna. The first to apply the model and publish was an assistant in Gottlieb's laboratory, Otto Preissecker, who extracted all three left upper molars in rats so that the left lower molars remained in a loss-of-occlusal loading status for six months (16). From a clinical perspective, which Preissecker refers to as the background behind his model system, a missing tooth simulation model addresses one of the most common problems in clinical dentistry: the changes in the dentition associated with the loss of teeth. Especially the loss of the first permanent molar is a common clinical problem observed in schoolchildren of industrialized civilizations. Once the first molar is lost, a number of changes occur within the remaining dentition. Among these clinical changes, the following are frequently observed: (i) distal drift of the adjacent premolars and mesial drift of the adjacent second molar, (ii) supra-eruption of the antagonistic molar, and (iii) tipping of the second molar and second premolar (17–21). The movement of adjacent and antagonistic teeth results in a narrowing and closure of the edentulous space (21). Tipping, drift, and supra-eruption may lead to tissue damage (22) and derangement in the patients' occlusal scheme (23).

For the Vienna School of Oral Biology, the un-opposed molar model system became a vehicle to test and support their biological concepts of skeletal biology, demonstrating that (i) that teeth were not statically attached to the jaw bone but rather constantly erupting, (ii) that tooth movement involved tissue remodeling rather than mechanical displacement, and (iii) that design and form of skeletal structures of the jaw apparatus, including the direction of tooth drift and other growth trends, were part of a species-specific functional and biological design of the skeletal system. Each of these questions is tightly linked to the intellectual evolution of the biological backgrounds of skeletal biology. Thus, the following chapters of this review are dedicated to the biological and historical aspects of the un-opposed molar model system as they relate to these questions.

Question 1: Do Teeth Erupt Beyond the Plane of Occlusion?

For the Vienna Oral Biology group, continuous tooth eruption was an example for a biological understanding of skeletal growth and was a step beyond the prevailing concepts of jaw mechanics of the early 20^{th} century. The first published report related to the eruption of teeth beyond the plane of occlusion is one of the many scientifically augmented clinical case reports that were published by members of Gottlieb's circle during the 1920ies and 1930ies. In one of these reports, Gottlieb described two cases of pseudo-shortening of a lateral incisor, in which the tooth in question was retained in a fixed position in the jaw due to failed root canal treatment, while the remaining teeth had further erupted beyond the plane of articulation (24). Gottlieb concluded that the non-treated teeth were subjected to movement in the years subsequent to root canal treatment of the reference tooth (24). Already three years later, in a landmark paper read before the Royal Society of Medicine, Gottlieb established his concept of continuous tooth eruption throughout life proposing that resorption and deposition within the bony tooth socket were responsible for the continuous eruption of teeth (25).

Gottlieb's report ignited half a century of debate between Gottlieb's Vienna School and Oskar Weski's and Richard Landsberger's followers in Berlin (26). The Vienna School argued that teeth were the driving force of tooth movement and would in turn induce alveolar bone remodeling during movement (24,25,27–30), while the Berlin group conceived tooth and periodontium including alveolar bone as a unity and found it impossible for the tooth to leave its support structures (27,31–34). In respect to the driving force behind the movement of teeth, Gottlieb favored the tooth itself (24) while Landsberger thought the alveolus was the source of tooth movement (31,32). Recent studies from our laboratory propose the periodontal ligament as a third alternative since levels of gene expression in periodontia of moving teeth were highest in the periodontal ligament (14,15).

After WWII, the discussion over Gottlieb's concept of tooth eruption throughout life was re-opened once more by anthropologists and archeologists (35). Briefly, archeological findings appeared to support the trend of continuous tooth eruption while concerns about periodontal status and tooth wear questioned some of the cephalometric reports (35). However, studies in populations with little or no wear have confirmed findings on continuous tooth eruption in human fossils (36–40). Today, almost a century after Gottlieb's original account, the Gottlieb-Weski debate appears to be settled, in favor of Gottlieb in regard to continuous tooth eruption throughout life, and in favor of Weski and Landsberger in regard to the unity of tooth and periodontium.

Question 2: Movement of Teeth: Mechanical Displacement or Tissue Remodeling?

Besides the question about the continuous eruption of teeth, the question about the biological mechanisms that lead to tooth movement was another vehicle for the Viennese to demonstrate the presence of orthogenetic "form follows function" principles in the design of the skeleton by using the un-opposed molar model (8,41,42). In the early days of orthodontics it was believed that during orthodontic tooth movement, bone behaves as a passive tissue that is continuously resorbed and apposited to adjust to forces exerted by the moving teeth ("bone bending theory")(43–45). Norman Kingsley (1829–1913), sometimes called the Father of American Orthodontics, wrote in his 1880 handbook entitled "Treatise on Oral Deformities as a Branch of Mechanical Surgery": "The movement of teeth in correcting irregularities is based on an anatomical and a physiological fact. The anatomical, that the teeth are placed upon the maxillae surrounded by vascular, elastic, bony processes, which are easily moved, absorbed, and reproduced; the roots penetrating but little into the true maxillae, and in their movement affecting the maxillae but slightly if at all. The physiological fact being that bone will yield or become absorbed under certain influences, and also be reproduced … In moving teeth the power used creates a pressure which produces absorption. The function of reproduction is nature's means of coming to the rescue and restoring lost parts." (43)

Kingsley's mechanical concept of orthodontia was replaced by a biological model of tooth movement through tissue remodeling in the early 20th century ("pressure tension theory") (46–48). Albin Oppenheim (1875–1945) frequently traveled to the United States, and became a regular lecturer at the Angle School of Orthodontia in Pasadena/CA. Through the Angle School, Oppenheim's biology-based concepts had an enormous impact on American orthodontics and led to the dawn of biologically-based orthodontic sciences in the United States, especially when the Angle School moved to the University of Illinois under the direction of Allan G. Brodie. Brodie's immense training abilities combined with a highly interactive oral biology faculty consisting of Isaac Schour, Joseph-Peter Weinmann, Harry Sicher, Balint Orban, Maury Massler, Julia Meyer, and others established the biological basis for orthodontics in the 1940ies, 50ies, and 60ies.

The establishment of a combined orthodontic oral biology research environment at Illinois allowed for the Viennese to perform and publish a series of key studies on the biological mechanisms involved in tooth eruption and tooth movement (8,13,41,42). These studies established precise measurements for the continuous deposition of mineralized tissues, including alveolar bone and root cementum, as major factors responsible for the movement of teeth (8,13,49–51). Most recently, the findings of the Illinois' Vienna scholars on tissue remodeling in the un-opposed molar system have been confirmed using contemporary techniques (14,15). In addition, these studies have identified the fundus of the alveolar crypt as a source for new periodontal tissue formation and as a powerful resource for periodontal tissue regeneration (14,15). While the debate over the cascade of events by which orthodontic forces induce tooth movement remains ongoing (52,53), the meticulous histological studies of the Vienna Group of Illinois have established the foundation to understand the contribution of tissues of the alveolar bone and root cementum toward tooth movement and tooth eruption.

Question 3: The Design of the Dentition - Genes or Environmental Adaptation?

The third and final question that the Viennese raised in respect to the un-opposed molar model was the question about the role of genes and environment in the design of the dentition. This question goes back to debates in turn of the century Vienna about genes, heredity, form and function. This debate in respect to tooth movement as it relates to the skeleton was re-ignited by a publication from another European émigré, Hermann Becks (1897–1962), who left Germany in 1928, established Oral Biology at the University of California at San Francisco, and coined the term "Oral Biology" (54) when establishing the American Institute for Oral Biology. In their modification of Preissecker's model, Becks and his co-worker Giorgio Cimasoni from the University of Geneva/Switzerland elaborated on the influences of function and heredity on the growth and development of the skeleton and referenced Wolff's law as it relates to the impact of function and paralysis on skeletal growth (55). Cimasoni and Becks' remarks about heredity and function as contributing factors in the design of the skeleton did not attempt to provide answers toward an understanding of their roles in tooth movement (56). However, it was exactly this question about the role of genes and environment in the design of the skeleton that triggered a sequence of studies related to the movement of teeth at the University of Illinois (13,50,51,57[; personal communication, Bernard Schneider]).

The reasons behind Sicher's keen interest in a model as simple as Preissecker's unopposed molar model becomes obvious in light of Sicher's background as a former assistant at the Ist Anatomical Institute (Lehrkanzel) of the University of Vienna. During this time and prior to joining Gottlieb, Sicher himself was an avid contributor toward Vienna's early 20th century debate over the role of form and function in the design of the skeleton using evolutionary and developmental model systems (58–66). Among these contributions, a vitreous critique of Otto Aichel's work on the evolution of tooth form (4) most tellingly reveals Sicher's intellectual heritage and position regarding evolutionary theories in Vienna and toward the problem of form and function. In his original publication, Aichel uses the extraordinary variability of fish dermal tooth forms (Fig. 5) as an argument to refute the concept of continuous evolution from fish to mammal and to question the concept of a functional adaptation of tooth form toward a nutritional environment. Based on the variability of tooth-like structures in the dorsal fins of catfishes of the genus Doras, Aichel argues for the superior role of variability over the concept of functional evolution of acquired characters. In his heated response (4), Sicher counters that Doras' fin-teeth are functional rudiments according to Darwin's terminology, which are characterized by great variability per se. He rejects Aichel's concept of the superiority of tooth form over function and instead argues for a continuous evolution of tooth form through functional adaptation toward ever-changing nutritional environments. Sicher repeatedly quotes Semon's mnetic engram hypothesis to explain the transmission and gradual functional adaptation of acquired functional traits throughout the evolution of the mammalian dentition (4). Even in later publications, Sicher returns to inheritance of mnetic characters as a heuristic principle to explain the problem of directed variation in the evolution of organisms and to the concept of orthogenesis as purposeful evolution of organisms (5). Today, Sicher's orthogenesis beliefs are certainly dated, but some of his basic ideas may be found in contemporary developmental plasticity concepts according to which environmental influences are thought to act upon an ancestral phenotype followed by a process of genetic accommodation (9).

Migration and Transformation of a Model System – Evolutionary Biology on the Move from Vienna to Chicago

When the Nazis came to power in Austria in 1938, several of Vienna's Oral Biologists relied on the long-standing collaboration between Chicago's dental schools and Gottlieb's Vienna Laboratory to find a home at the University of Illinois and at Loyola University College of Dental Surgery (67). Incidentally, 19th century Vienna's questions about genes, evolution, development, and heredity became centerstage once more when Harry Sicher and Joseph-Peter Weinmann arrived in Chicago in 1939 (Fig. 6). Leaving Vienna's 9. Bezirk (Alsergrund) and the timeless discussions in Vienna's Old Rifle Factory, the Austrian Scholars now moved to the 14-floor U of I dental school tower in Chicago's Medical District. The Windy City soon became a nurturing ground for the intellectual and scholarly ambitions of the Viennese. Through their biological approach and through books such as "Bone and Bones" and "Orban's Oral Histology and Embryology", the European émigrés had great impact on post-war medical and dental education. During the mid-30ies, Chicago had largely recovered from prohibition era gang warfare that overshadowed the City since the introduction of the 1919 Volstead act. At this time, Chicago prided itself with three of America's leading dental schools, Northwestern University Dental School, the University of Illinois College of Dentistry, and Loyola College of Dental Surgery. Collaborations and interactions within the City flourished, especially with the University of Chicago and Chicago Medical School.

In this sizzling environment mirroring aspects of Vienna's former intellectual wealth, even Chicago's architects, Louis Henri Sullivan and Frank Lloyd Wright, echoed Vienna's motto "Form ever follows function". With the arrival of Orban, Sicher, and Weinmann, Vienna's debate over adaptation and selection, over ontogenesis and phylogenesis, over genetics, evolution, and function, and over Lamarck, Haeckel, Hering, Semon, Weismann, Mendel, and Tschermak, was transplanted into the new faculty offices of Chicago's dental schools. In the minds of Vienna's distinguished group of Oral Biology émigrés, Vienna's discussions were once more applied using craniofacial model systems. At the University of Illinois, two deans, Allan G. Brodie (Dean from 1944–1955) and Isaac Schour (Dean from 1955–1964), supported and encouraged the work of the Vienna group in the U.S., and also interacted scientifically with the Viennese. Especially graduate students from Brodie's prestigious Department of Orthodontics worked with Julia Meyer, Joseph-Peter Weinmann, and Harry Sicher as mentors on their thesis projects. As a consequence, the model systems related to tooth movement, eruption, and occlusion, imported by Sicher and Weinmann as a memoir of their Vienna times, experienced a renaissance in Chicago's dental research community during the 50ies and 60ies.

In Chicago's New Vienna at Lake Michigan, questions about the driving force behind the design of the dentition took center stage once more. This time, Sicher and Weinmann confronted a young student in Brodie's Orthodontic Department with the question about the reason for the anteroposterior movement of teeth (drift)(Bernard Schneider, personal communication). Sicher explained that in rodents, teeth drift in distal direction, while in humans, teeth drift toward the center front of the skull (mesially)(Fig. 8). "Environment or genes?" the Vienna masters wanted to know – was it the form of the occlusal relief or were genetic traits responsible for the direction of the drift? Or in 19th century Vienna terms: "Does tooth form determine function or does tooth function follow a genetically determined form?" The mesial inclination of human molar tooth roots toward the plane of occlusion and the distal inclination of upper rodent molar tooth roots toward the plane of occlusion supported the genetic argument; while the physical orientation of occlusal surfaces supported the notion of an environmentally determined drift pattern. "Why don't you remove the occlusal surfaces of the teeth in one quadrant and you'll know," Sicher asked, well-aware of Preissecker's model from his time at Gottlieb's Institute in Vienna. For Bernard Schneider, the young student in Brodie's Department, a research project was born (Fig. 2).

A decade later, when Schneider was ready to publish his results, Weinman was already deceased and while Sicher's health allowed only occasional visits to UIC's College of Dentistry. In the meantime, their close associate and Swiss émigré Julia Meyer had taken over the mentorship for Weinmann's graduate students at the University of Illinois in seamless transition. At Illinois, Preissecker's and Cimasoni and Beck's descriptive histological analysis was replaced by a thorough and systematic approach using morphometric statistics and vital dye staining techniques that had been introduced decades earlier at the same University by fellow faculty members (68,69). As such, their measurements focused on the remodeling of tissues such as alveolar bone, periodontal ligament, and cementum, and their questions were intimately linked to the clinical and intellectual backgrounds of their mentors Brodie, Schour, Sicher, Weinmann, and Meyer (13,50,51,57). The scope of these post-war Chicago studies confirms that the studies undertaken were a direct reflection of Chicago's intellectual environment and the techniques available at the University of Illinois at that time. As faithful gatekeepers of Sicher and Weinmann's intellectual heritage, Schneider and Meyer's investigation was driven by a search for answers to Sicher and Weinmann's questions about the role of form and function in the evolution of the dentition. In answer to these questions, they studiously reported that molars had drifted in distal direction following relief of occlusion and that this "…finding directly contradicts theories of horizontal tooth movements based on functional forces as the causative agent." (13). In order to explain the observed changes in tooth position, they suggested a "high potential of alveolar bone growth" and "an inhibitory regulating mechanism which resides in the animal's own masticatory activity and through which alveolar bone formation and tooth movements are adjusted…" (13). Schneider and Meyer were proposing that the functional design of the rodent occlusal surface would have pressured teeth to migrate in mesial direction. Thus, half a century following Otto Aichel's and Harry Sicher's debate over form and function in World War I Europe, Sicher's stance had once more returned to Vienna's neo-Lamarckian orthogenesis concepts: not tooth form determines function, as Aichel had proclaimed, but anteroposterior tooth movement is a genetically determined feature subjected to various function-valued evolutionary pressures in different mammalian orders.

Thus, Vienna's debates over form and function, and over the mechanisms of skeletal evolution are as much alive today as they were 100 years ago. Today's debate over the role of genes and environment on phenotypes centers on questions related to genetic determinism and developmental plasticity. Today's challenge is to determine just how much of a future phenotype is determined by genes, totally random variation, and selection in contrast to the inheritance of basic features reflective of adaptive responses with an evolutionary history. One approach to address these questions will be to link environmental, genetic, and phenotypic variation to selection and evolution through mediation of gene expression (9).

Conclusion - Cultural and Methodological Paradigms as Vehicles of Scientific Progress and Systems Biology

We have told the scientific history of the un-opposed molar model from fin-de-siecle Vienna to post-WWII Chicago as it evolved from a simple clinical observation to a model for tissue regeneration and genomic biology. In their exile community in Chicago, a group of Viennese Oral Biologists used this model system to address science philosophical questions about evolution and heredity and about the influence of genes and environment that were first developed in late 19^{th} century Vienna. Today, the scientific questions related to the roles of genes and environment as they influence evolution and morphogenesis have surfaced once more in the debate over the roles of genetic determinism and developmental plasticity as they relate to phenotypic change. As such, the scientific history of the unopposed molar model is a beautiful example of a cascade of paradigm shifts in Kuhn's sense accomplished by technical advances in tandem with changes in cultural context as postulated by methodical culturalism (70–72).

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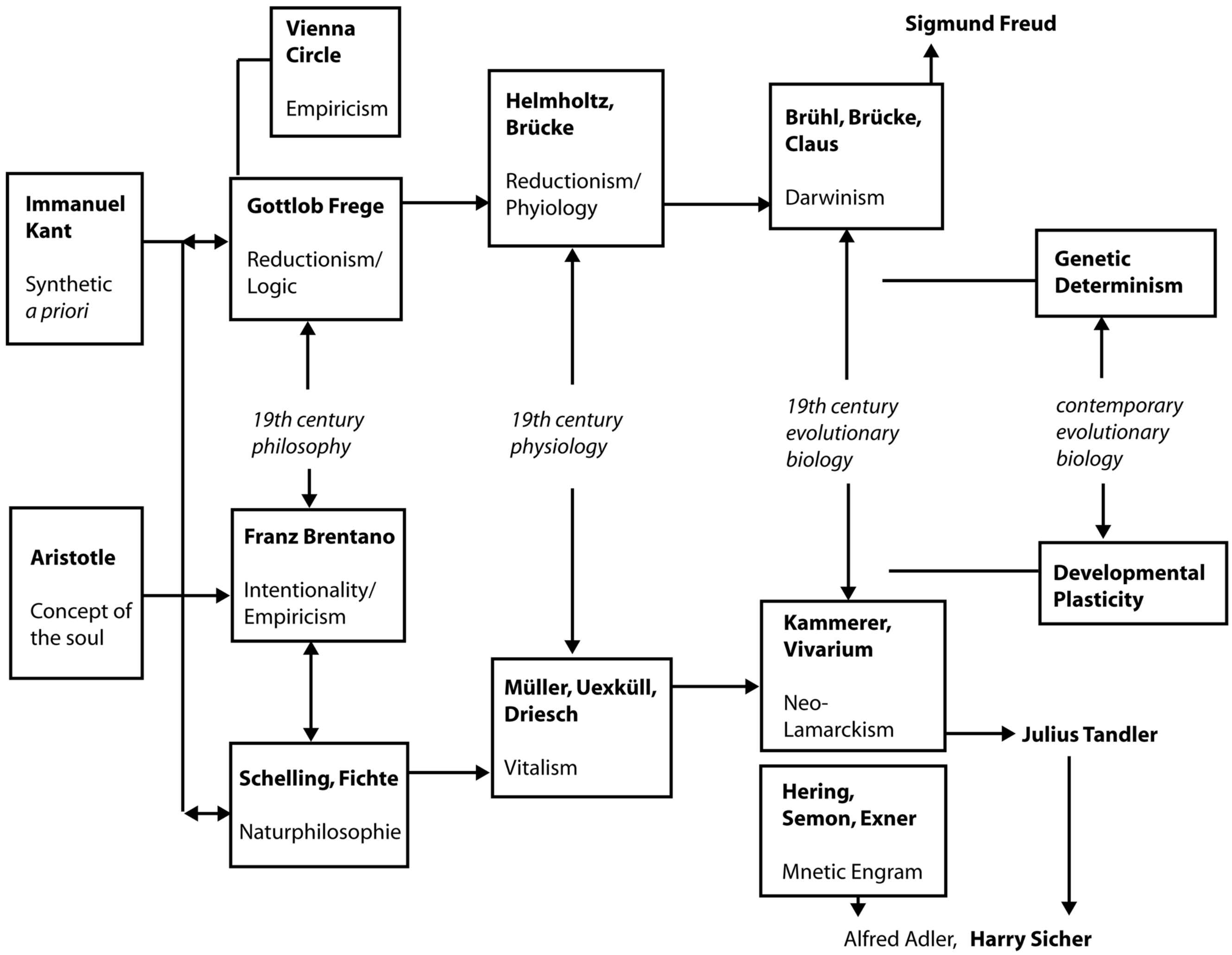

Figure 1.

Trends and schools in biological philosophy from 19th century Vienna until today. 19th century science philosophy in Vienna centered on questions of heredity and empiricism and their interpretation in relationship to classic concepts of Kant and Aristotle. The resulting opposition between reductionism and vitalism also impacted the interpretation of evolutionary theory. 19th century debate over the influence of genes and environment on heredity is somewhat mirrored today in the discussion between genetic determinism and developmental plasticity albeit the terminology of genes and our understanding of environmental influences has changed.

Figure 2.
Science-historical and intellectual bridges between distant academic realms. Fig. 2A. Alfred Adler (1870–1937), Viennese psychiatrist and father of Individual Psychology. Adler's holistic psychology and its connection to 19th century Naturphilosophie had a profound impact on the young Harry Sicher, his philosophy of life, his approach toward evolutionary theory, and the scientific questions about the growth of the skeleton that he would ask throughout his scientific career. Fig. 2B. Peter Janich, prominent science philosopher from the Philipps-University of Marburg/Germany and father of methodological culturalism. Janich was the first to emphasize the importance of methods, model systems, scientific language, and cultural context on scientific thought. Fig. 2C. Bernard Schneider, Clinical Professor of Orthodontics and the last

student of Harry Sicher and Joseph-Peter Weinmann at the University of Illinois. As an oral history witness, Schneider vividly recalls the keen interest of the Viennese émigrés in questions related to the influence of genes and environment on the evolution of the dentition, as reflected in Schneider's postgraduate research on the un-opposed molar model system (Schneider et al. 1965).

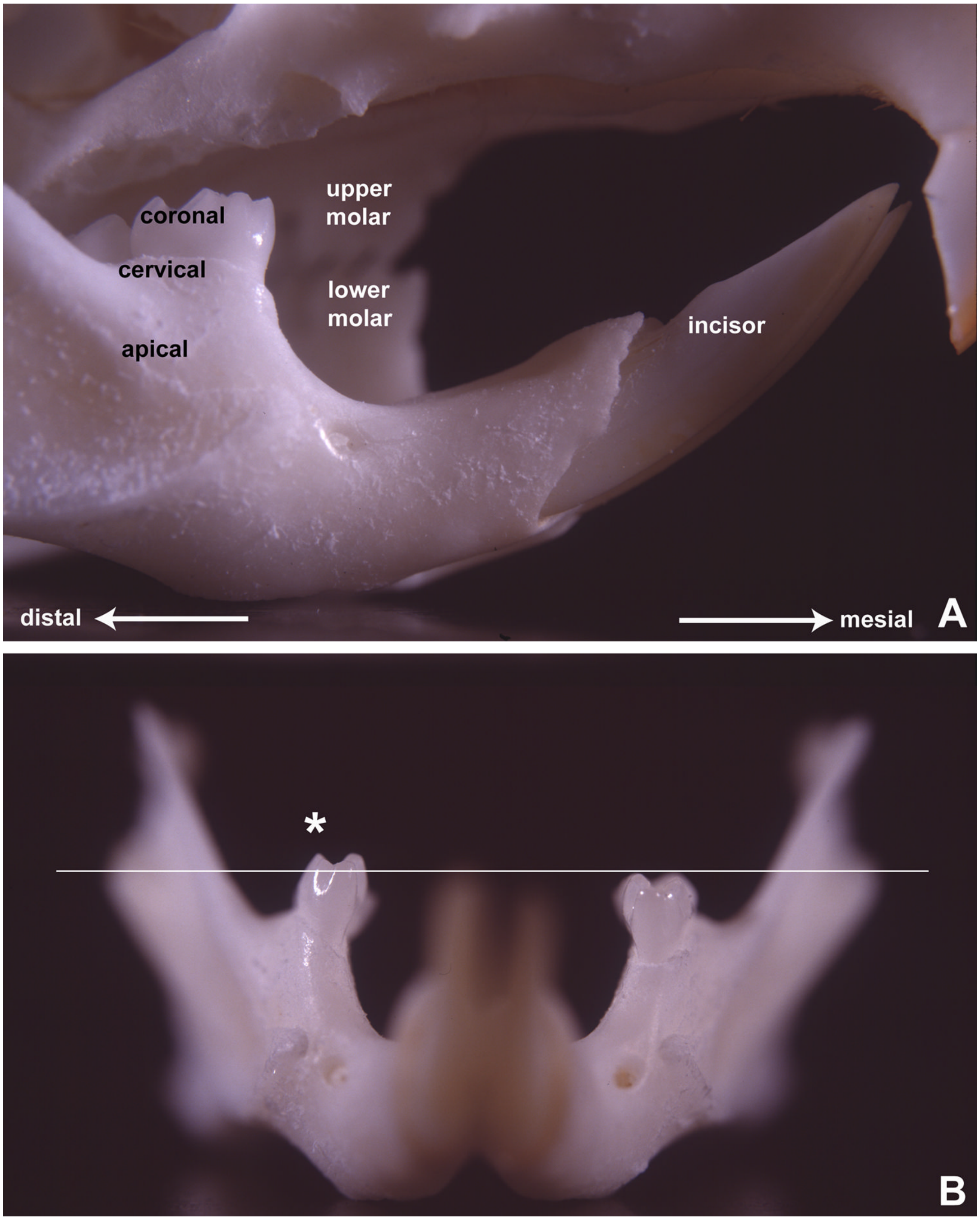

Figure 3.
The model system of the un-opposed molar – the focus of Sicher and Weinmann's interest in the evolution of the dentition during the last years of their distinguished exile careers at the University of Illinois. Fig. 3A. An un-opposed occlusal situation in the lower jaw is created by extraction of the antagonistic upper molar teeth (asterisk). Mouse dentitions feature three upper and three lower molars on each side of the jaw. Four continuously erupting incisors protrude into the anterior portion of the oral cavity, one in each quadrant. The anterior aspect of a tooth is called mesial while the posterior aspect is called distal. Three regions of a fully erupted tooth are distinguished: The coronal portion, which describes the area of the tooth crown, the apical portion, which is directed toward the tip of the root of the tooth (apex), and

the cervical portion, which is located at the interface between tooth crown and tooth root. Fig. 3B. As a consequence, molars of the lower jaw super-erupt beyond the plane of occlusion (asterisk). Tooth elevation during a period of 12 days amounts to 0.13mm.

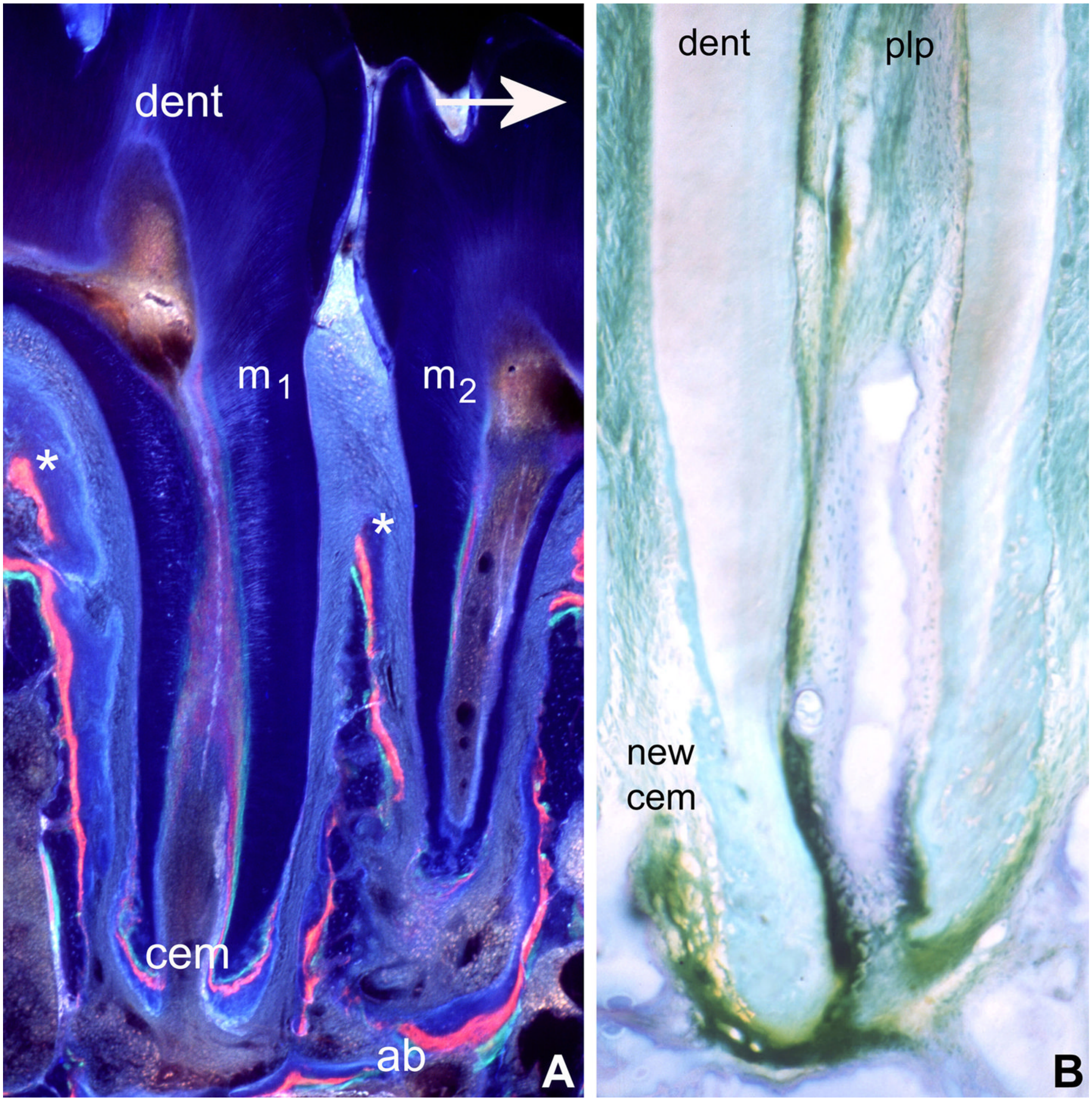

Figure 4.
Peri-apical tissue regeneration as a consequence of lack of occlusal forces. Fig. 4A is a micrograph of an ultrathin ground section revealing 4-day intervals of mineralized tissue apposition via vital dye labeling. There was massive new alveolar bone deposition at the distal alveolar walls (asterisk) as a cause for distal drift of molar teeth in rodents (arrow). Note the formation of new alveolar bone (alv) and cementum (cem) in the periapical region of molar tooth roots (Fig. 4A and B). M_1 is the distal root of the first mouse molar, M_2 is the mesial root of the second mouse molar. The direction of the drift is indicated by an arrow. Crown dentin (dent), dental pulp (plp) are labeled for orientation purposes.

Figure 5.

The evolutionary forces behind the multitude of shapes and forms among the dermal teeth in catfishes of the genus Doras were the focus of a heated debate over the role of variation and function in the evolution of organisms between Otto Aichel (1871–1935) of Kiel and Harry Sicher of Vienna. As primary causes behind the evolution of skeletal features, Aichel favored the natural variability of forms and shapes while Sicher advocated the “form follows function” concept, echoing generations of Viennese functional anatomy tradition as well as holistic concepts of heredity. Catfishes display a wealth of dermal armor, as depicted here in the multitude of tooth-like structures on the skin and fins of the Giant Clawed Catfish (Pseudodoras niger = Turushuqui). Aichel’s and Sicher’s argument was about the evolutionary mechanisms that might have lead to the formation of such highly refined structures that defy any functional explanation at first sight.

Figure 6.
A New Vienna at Lake Michigan. The Vienna group of Illinois as they are known best to generations of American dental students (from left to right): the Pedodontist Maury Massler (1912–1990), the Periodontist Balint Orban (1899–1960), Dean Isaac Schour (1900–1964), the Oral Pathologist Joseph-Peter Weinmann (1896–1960), and the Anatomist Harry (Harald) Sicher (1889–1974). The textbooks of the Viennese émigrés became standards for Dental Education in America and shaped the biological foundation of American Dentistry forever.

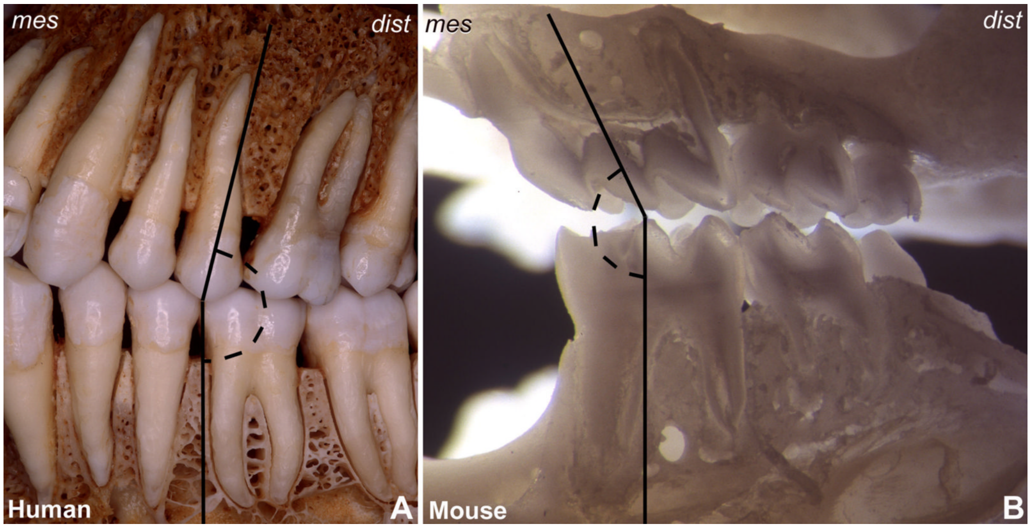

Figure 7.

The drift of the dentition in rodents and men. Note that in humans, the roots of molars are inclined in distal direction, while in mice, the upper molar roots point in steep mesial direction. The opposite inclination orientation between the tooth roots of mice and men and their possible role as a genetic factor influencing tooth drift became the basis for Harry Sicher's scientific reflections on the role of genetic and environmental factors as they relate to the ontogeny and phylogeny of the skeletal system.