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What Causes Curly Hair?

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Synopsis

We do not know what causes natural-born curliness in human scalp hair or in the hair of mammals in general. This brief review describes why hair curls, and the cause of the phenomenon is more complex than often appreciated. We then briefly review features that are associated, correlated, or purportedly cause hair curl.

INTRODUCTION

"Eat up your bread crusts children, so that your hair grows curly." —Traditional

This old British saying was more about food wastage than hair. However, crusts aside, the causes of and influences on hair curl are still not completely understood. Here we briefly review current work in this area and explain why answering the deceptively simple question of "what causes curl" remains a challenge.

WHY DO WE CARE?

We notice hair. Lack of hair, color, texture, and style of hair provide visual information from which our brains subconsciously extract useful social information, such as individuality and conformity to norms. Hair is a tricky signal of anything at a truly biological level (e.g., health status, fitness, or fecundity) because it is easily customized, and, in addition to clothing, hair is the feature that we most readily change temporarily to express ourselves (1). All of this is an important part of our psychology, especially of physical attractiveness (2,3).

Curliness is not only an important component of hair style (4), it also has implications for technical performance, especially for people with very curly-textured hair, because of an increased tendency to catch and tangle (5–7). The fur coats of most mammals also rely on some hairs being curly to fill space and trap air for insulation (8,9). In domestic animals, such as sheep and angora goats, hair curliness (related to properties called crimp and bulk) has implications for the uses and value of their wool and the survivability of livestock in different environments (10). As a biomimetic model for protein-based shape memory materials, curly and straight hair could play a key role in informing the

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development of new bio-based materials composed of keratin and other similar fibrous biomolecular assemblages (11,12).

WHAT IS CURL?

Curliness can be intrinsic or induced. Here our focus is on intrinsic curliness. Intrinsic curliness is the shape built into a hair shaft during its growth in the follicle, and it is this shape to which an untreated hair returns when relaxed in water and dried without mechanical constraint (13). Imposed curvature is any chemically or physically induced change to intrinsic curvature, for example, from drying a fiber in a constrained state, heating a fiber in a constrained state, or inducing disulfide exchange via a permanent set technology (4). For an individual's hair, the intrinsic curliness is what induced changes must build upon, and it is this intrinsic scenario that we still do not fully understand.

What shape is curliness? For a single hair shaft, curl is three-dimensional and varies along its length. Curl is therefore a coil, something like a spring, at any one point along its length. Describing three-dimensional curliness mathematically requires each point along a hair to be described in terms of curvature and torsion (14) (Figure 1A). Measuring unconstrained hairs in three dimensions is time intensive and expensive (Figure 1B). However, constraining fibers into two dimensions and measuring only curvature is quick and relatively inexpensive. Constrained curvature data have proven to be relatively comparable to the extent that the

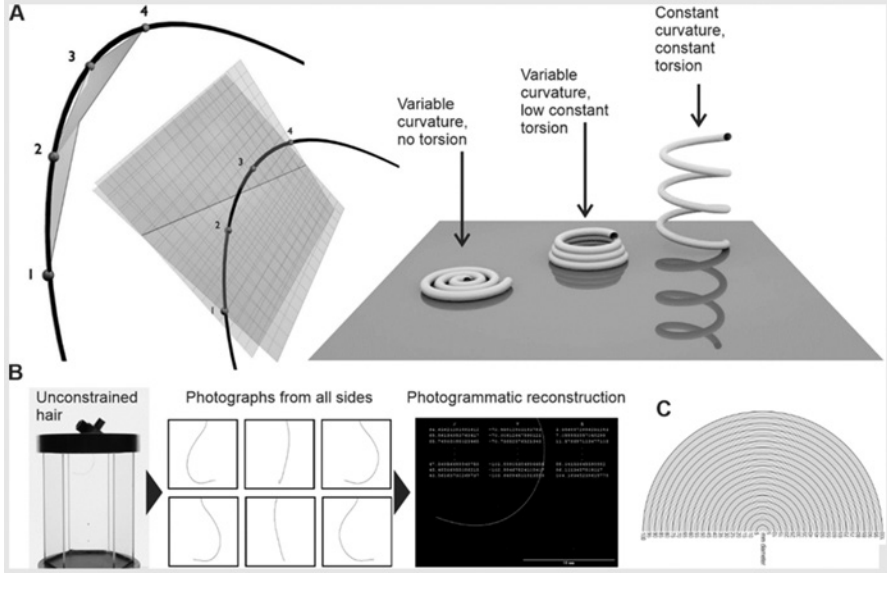

Figure 1. Measuring curliness. (A) Curvature and torsion are three-dimensional components of hair curl. Curvature is measured on a plane that is defined by three points. Here curvature is measured on the infinite plane defined by points 1, 2, and 3, and the plane defined by points 2, 3, and 4. Torsion at midpoint between 2 and 3 is the angle between the two infinite planes (1, 2, 3 and 2, 3, 4) divided by the distance between 2 and 3. Some examples, of varied curvature and torsion. (B) Example of a photogrammetric approach to three-dimensional hair shape using photogrammetry. (C) Example of a radial ruler against which constrained hairs are placed to measure curvature quickly.

data have become the basis of standard measurements in both the wool and hair industries. In the wool industry, automated microscopy techniques (notably the optical fiber diameter analyzer) rely on measuring curvature from small subsamples of single fibers from within multifiber "staples" (a tress) and generating curvature in units of degrees per millimeter (15). In hair research, the routine approach is to constrain single hairs under a transparent sheet and line up hairs against a circular ruler to give a radius or diameter in millimeters or centimeters (Figure 1C). Loussouarn et al. (16) developed a curl classification system based on hybrid measurements where curl diameter was augmented by other simple two-dimensional measurements that indicate elements of the three-dimensional shape of a hair, including along-hair variability. Combining measurements in a statistical model allowed origin-independent classification of hair curl into a system of type I (straightest) to type VIII (most three-dimensionally curly).

DIFFERENT TYPES OF CAUSATION AND NONCAUSATIVE CORRELATION

The question "what causes and influences hair curl" is more complicated than it first appears. Causation occurs in multiple contexts. Curvature and torsion in a mature, dead, hair shaft are caused by the chemistry and structural organization of the shaft. That shaft structure was caused by processes during hair growth in the follicle, including the spatiotemporally distributed processes of keratin maturation and cornification. Ultimately, germline genes and physiological factors defined the follicle's program to grow a hair of specific curliness, with this cause being first implemented during embryogenesis and then reconfigured by successive cycles of telogen and anagen.

What causes curliness at the level of inherited genes may be of little interest to on-the-head product developers, but the cause of curliness at the level of the hair shaft itself might inform new technology. Conversely, dermatologists, anthropologists, and forensic scientists will differ in what level of causality is relevant.

Irrespective of whether we are investigating curliness at the level of the hair shaft, hair growth, or follicle cycle, causation occurs within a complex system. A hair shaft contains multiple layers (i.e., medulla, cortex, and cuticle) and sublayers (e.g., orthocortex, paracortex) that were derived from once-living cells (17). Within the cortex, for example, hair shaft structural organization can be described over a wide range of spatial scales, with each having potential contributions to fiber structure and mechanical properties. These include protein chemistry (e.g., the matrix and the keratin intermediate filaments it surrounds), the architecture of filaments into macrofibrils, and the overall fiber shape.

Within an anagen follicle, the situation is more complex again because the follicle is a miniature organ that creates a tissue that then cornifies into a range of different hair morphologies. Mammalian hair diversity indicates that a wide range of functional fibers can be produced by a follicle. While investigating causes of curliness, we should therefore be mindful of the following:

- Curliness may have multiple potential causes (e.g., fiber ellipticity, cortical organization).
- The multiple causes may be nonexclusive; therefore, a specific curliness is an emergent phenomenon (i.e., the sum of causes).
- There may be features that correlate with curl, but do not cause curl, that are caused by a common third phenomenon.

As researchers have come to realize that hair shaft properties may be emergent rather than due to a single cause, it has been recognized since the early 2000s in wool (18) and more recently in hair (19,20) that this requires investigation using a systems biology approach. Within this complex system, we expect to see some phenomena that correlate with curliness but do not cause curliness. This is a common problem in biology called a spurious correlation. A version of the issue was popularized by Gould and Lewontin (21) in the context of evolutionary biology. In the context of fiber growth, for example, various studies find that both the expression of inner root sheath keratins (22) and hair shaft ellipticity correlate with hair curl (23,24). But, does the keratin expression cause the ellipticity, or is it a consequence of ellipticity because follicles have a circular cross-section, and the inner root sheath fills in the difference between ellipse and circle? Or are both caused by a common causative mechanism, such as the organization of the neck of the dermal papilla that orchestrates the fate of cells into the various lineages including shaft and inner root sheath during hair growth (25)? This particular issue was first raised by Priestley (26), and despite decades of additional data slowly filling in our understanding of follicle biology, we still do not know the answer to this example question. An experimental approach is essential to directly tease out noncausative correlations from causation in addition to comparative analysis.

WHAT FIBER FEATURES CORRELATE WITH CURL?

WITHIN THE MATURE HAIR SHAFT

Internal organization of the hair cortex, follicle morphology, the shape of the fiber cross-section, and differences in protein abundance have been described in the literature as features that correlate with curl. For more than 90 years, researchers have been trying to work out how fiber curvature correlation with mammalian hair features might explain a mechanism causing curliness. Studies have largely focused on three contexts: human scalp hair, midside wool from sheep, and mice (typically as models of genetic disorders affecting human scalp hair). Although there are some common features that correlate with hair shaft curl in scalp hair, sheep wool, and mouse hair (plus other species), the differences are particularly informative for identifying and discounting features underpinning hair curliness in all mammals. For example, studies of human scalp hair often point out that curly hair shafts tend to have a more elliptical cross-section than straight hairs (27–29). Ellipticity alone is not a mechanism, but could an elliptical profile be immutably connected to the process that generates curl? Sheep wool indicates that this is not the case, and there are clear examples of the reverse situation where hair shafts from merino and merino relatives that have a more elliptical profile are less curly than those with circular profiles (30). This demonstrates the challenge of correlating just one feature with curl.

It has been appreciated since the 1950s that cell-type distribution in the cortex region of the fiber correlates with various measures of hair curliness (31). Sheep wool with lower-diameter hairs (15–25 μm) is the most curly and has been investigated as a model to study fiber curvature because it is made of three distinct modes of keratin organization (ortho-, meso-, and paracortex) embodied within macrofibrils composed of keratin intermediate filaments and matrix (32,33). The macrofibril-containing cells of the hair shaft, once living in the follicle, now dead and transformed to structural elements in the mature hair, are

themselves typed as ortho- or paracortical (or sometimes mesocortical). In high-curl wool fibers, such as those from the merino breed, the paracortical cells are clustered along the concave margin of the cortex, forming a strip with orthocortex on the convex side. The relation between cell type in low-diameter wools has become a definition applied to hair from other mammals. However, the direct transfer of wool cortical terminology to other hairs has been an oversimplification. In human, goat, alpaca, rabbit, deer, and higher-diameter sheep fibers (25–50 μm), cortical cell types can be ambiguous in both chemistry and structure, and single cells can contain macrofibrils of multiple architectures (10,17,32–34). In particular, while the traditional view is that the intermediate filaments making up paracortical and mesocortical macrofibrils are arranged in parallel arrays, while those of the orthocortex are twisted into rope-like columns, recent studies show that the intensity of twisting varies. This variable twist means that many cortical cells contain features associated with both orthocortical and paracortical cell types.

The details of cortical cell types are important because their organization not only correlates with curvature but has also been implicated as part of proposed mechanisms of curvature. Munro and Carnaby (35) developed a mathematical model that described how differential contraction of the cell types can explain fiber curvature in wool. Their hypothesis assumes that the fiber in the follicle is in a moisture-saturated state, and when the fiber dries during the transition to the mature state, the matrix located between intermediate filaments shrinks laterally. Because orthocortex is composed of helical wound ropes of intermediate filaments, lateral contraction should affect intermediate filament tilt and macrofibril length differently than in the paracortex. The resulting differential contraction then strains the fiber to curve toward the paracortex.

With the Munro and Carnaby model in mind, studies on wool fibers have looked at differences between the orthocortex and paracortex using light and electron microscopy (13,36), atomic force microscopy (37,38), electron tomography (33,39,40), genomics (41,42), proteomics (43–47), microbeam small angle x-ray spectroscopy (48), elemental (49), and thermal analysis methods (50,51). The data have informed further models (52,53). Largely these studies have supported the models, but there have also been some findings that challenge the models, such as the discovery that macrofibrils can have variable tilt (46), that the proportion of orthocortex and paracortex does not correlate with curvature (13,51), and instead that the relative difference in length between orthocortical cells close to the outside of the curvature and paracortical cells close to the inside of the curvature correlates to curvature at that point in the wool fiber (13). Despite these new findings, the Munro and Carnaby–type models remain a good conceptual foundation for explaining curl in wool fibers.

However, in human hair, the bilateral cell-type distribution is not typically observed in the cross-sectional images as it is in low-diameter wool fibers. Underlying this is the fact that cortical cell types are not as clearly differentiated in hair as they are in wool, and this occurs at the levels of macrofibril structure (33), cortical cell types and microscopy staining chemistry (33,39,54,55), and in intermediate filament angles (56). Historically, human scalp hair cortex has been described as the same as for wool (57,58), as orthocortex only (59), as like but not identical to wool (56,60), or using new terms (e.g., meta- or heterocortex) (61–64). Using a bespoke classification for human hair based on differences in macrofibril appearance using transmission electron microscopy, fluorescent stains, and electron tomography, Bryson et al. (39) demonstrated that differences analogous to those seen in wool in the cell-type distribution also occur in moderately curly and straight scalp

hairs. In the straight fiber, the cell types were arranged annularly and evenly within cortex, implying that the averaging of differing structural features would maintain a straight fiber conformation. In the curly fiber, the cell types were bilaterally distributed approximately perpendicular to fiber curvature direction. Previously, this pattern had only been observed in human scalp hairs with extremely high curliness (65). Among low-diameter mammalian hairs, fiber curvature is generally correlated to differences in cortical cell-type distribution across the cortex, with straight hair shafts containing an annular cell-type distribution and curly shafts a more bilateral distribution (46).

WITHIN THE FOLLICLE

Whatever the cause of curvature is at the level of the hair shaft, that cause originated in the hair follicle and resulted from a program of events that started within the living cells at the base of the anagen follicle bulb (24,66,67). Unlike correlations with curliness in the hair shaft, many of the correlations observed at the level of follicle structure have led directly to hypotheses of causation. It has been proposed that the shape of the hair follicles largely determines the shape of the fibers. Curly hairs from humans (regardless of ethnicity) and sheep typically emerge from curved follicle bulbs and straight fibers from relatively straight follicle bulbs (24). This has led to a common perception that hairs are extruded and take on the form of the follicle that produced them. In the middle of the 20th century, there was an awareness that follicles were in a dynamic state, mobilized by their arrector pili muscle (68). This led Chapman (69) to propose that muscle-induced rotation of the follicle bulb might cause hair shaft curl. However, the extrusion hypothesis is largely discounted based on more recent microscopy studies of follicles. Not only do follicles have a retrograde curvature (the bulb curves the opposite direction to the final fiber), but straight fibers have been observed growing from curved follicles in cultured bovine follicles, indicating that the correlation between follicle morphology and fiber curvature may be noncausative but associative (70). Rather than a cause, follicle bulb curvature may be a consequence of fiber development, such as different rates of protein expression across the cortex (71), cell reshaping and migration (72), or simply redistribution of stresses in a high-pressure biological environment (73).

Other features that correlate with, or are associated with, follicles that generate curly hairs are differences in cortical keratin expression patterns (74) and in ultrastructural assembly of macrofibrils (75). Thibaut et al. showed using *in vitro* growth that curly hair is programmed in the basal area of the follicle, so asymmetry of keratinization was believed to result in a bilaterality of cell-type formation. Also associated with curly-hair–producing follicles is that the outer root sheath and the connective tissue sheath lack symmetry along the follicle (24). This is also known for wool, where the thicker outer root sheath associated with the concave curve of the follicle bulb is called the ental side and the other the ectal side of the follicle (68).

Asymmetry of follicle morphology associated with hair curvature may have led Hynd et al. (76) to propose a model in which asymmetrical cell production on either side of the dermal papilla combined with a staggered initiation of keratinization and hardening on different sides of the hair shaft caused curvature. Work by Harland et al. (13) has challenged the role of asymmetric cell division as a cause of curvature in high-curl wool fibers, but the concept of staggered hardening remains intriguing. Further investigation tracking cells during

their transit through the follicle will likely be required to identify additional potential contributions of cell division, migration, and reshaping to curvature.

PROTEOMIC AND PROTEIN EXPRESSION

Our ability to both identify and relatively quantify individual structural proteins and their chemical modifications and associations (e.g., chemical cross-links) between hair samples is rapidly developing. The current state of knowledge from sheep model studies is that the abundance of some structural proteins differs between straight and curly wool fibers from closely related individual animals (fraternal twins). Quantitative mass spectrometric analysis demonstrated that straight wool and curly wool differed in the relative abundance of individual species from high glycine-tyrosine protein families and ultra-high sulfur protein families (46). Similarly, protein abundance differences have been observed between human scalp hair samples chosen for being very straight versus very curly (77). Proteomic analysis was able to pick out individual keratin and keratin-associated proteins that differed between the sample groups (keeping in mind that samples likely differed in other ways than just curliness). Quantitative mass spectrometry is a rapidly advancing technology, and these early results suggest it will be a powerful tool to identify the proteins of interest for understanding phenomena such as hair curliness. The main current limitation of all mass spectrometry techniques is that optimal results require multiple hairs and a lack of data on protein associations or locations, although both of these are areas of current research (78,79).

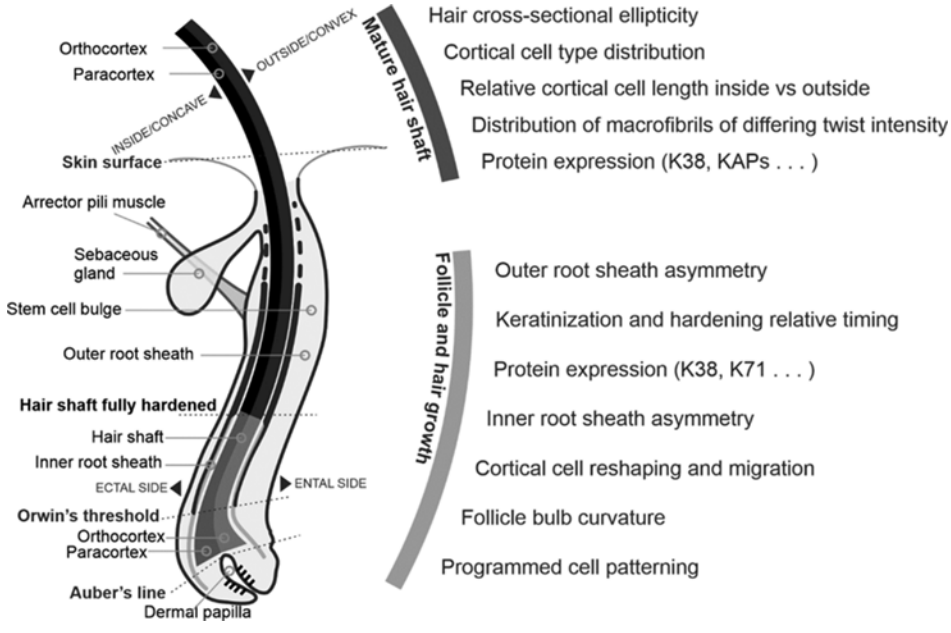

Figure 2. Summary of a generic mammalian anagen phase follicle growing a curly hair, with key structures and features associated with curvature listed.

Proteomic analyses of follicles are few (80). Genomic analyses of curly versus straight hairs have identified single nucleotide polymorphism targets associated with curly hair or curl-associated mutations (27), but protein analyses at the follicle level have largely been carried out using techniques that target specific proteins and determine their location. Most advances have been made using in situ hybridization and immunohistochemical approaches (44,67,74,81–84), and few have targeted understanding curl. However, work on both human scalp and wool follicles indicates the association of K38 with increased expression on the ental side of the developing cortex in high-curl hair (44,58,74).

CONCLUSION

The future challenge will be to connect the many factors in hair and follicle (Figure 2) that correlate with the presence of hair curliness or the extent of curliness. This will require linking features through chemistry and biology to morphology across scales from microscopic to macroscopic and will require an experimental approach and likely correlative measurements (e.g., the three-dimensional location of protein chemistry in fiber and follicle).

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