

THE ROLE OF CURVATURE IN ENTANGLEMENT

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Which tangles more readily: curly hair or straight hair? A perhaps natural thought, supported by some theoretical evidence, is to associate curvature and entanglement, and assume that they would grow together - that an increase in one fosters an increase in the other. However we have biological examples such as DNA in the chromosome, and mechanical examples such as coiled telephone cords, in which much more curvature is employed than is required for the packing, and in which tangling is presumably detrimental.

We offer a resolution to this conundrum. We show, that at least for simple but generally applicable models, the relationship between curvature and entanglement is subtle: if we keep filament density constant and increase curvature, the entanglement initially increases, passes through a maximum, then decreases, so there is a regime where increasing curvature increases entanglement, and there is also a regime where increasing curvature decreases entanglement. This has implications for filament packing in many circumstances, and in particular for the compaction structure of DNA in the cell – it provides a straightforward argument for the view that one purpose of DNA coiling and supercoiling is to inhibit entanglement. It also tells us to expect that wavy hair –neither the straightest nor the curliest – tangles most readily.

How would one best pack a long string into a small volume so as to minimize tangling? A little thought tells us that we could accomplish this by inhibiting the motion of the string entirely. However, in many circumstances this is not possible; often, as in the cases of the DNA and the suddenly obsolete telephone cords mentioned above, because motion is required for the purpose or function of the string.

In particular, DNA in the cell lives in a fairly volatile environment – there are free radical collisions which can cause breaks in the string, sections of the string must be manipulated and exposed for RNA copying, and of course the entire string must be unzipped and replicated for mitosis (cell division). To address these happenings and others, there is constant enzyme activity – cutting, joining, copying, repairing the string. All of these effects, and others, can lead to tangling and DNA tangling can cause, among other things, cell death [7]. There are several families of enzymes, most prominent of which are the topoisomerase, which address this tangling problem.

Many of our everyday filaments, such as hair and electronic cables, while they are not frequently cut and repaired, are also in dynamic environments.

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In sum, this means that we can expect some noise or stochasticity to play a role in the filamentary behavior. So perhaps our question is better stated as: how would one best pack a long string into a small volume so as to minimize tangling, given that there will be some motion and stochasticity involved? The curvature is a local property of the filament, one of the fundamental descriptors of any filament, and so is natural as a first focus point in these sort of problems. For example, there has been considerable interest in the curvature of DNA[11][12][1][5][13][14].

Some basic connections between curvature and entanglement have been found. Milnor [15] showed that any knot in a closed loop would require at least 4π of total curvature, where total curvature is defined as the integral or sum of the curvature over the length of the knot. One might think from this that entanglement patterns of increasing complexity require increasing curvature (here and henceforth by curvature we mean total curvature). However, as was shown in Buck-Simon[6], this is not the case, one can have knots of arbitrarily high complexity, as measured by crossing number, with curvature $4\pi + \epsilon$, where ϵ is an arbitrarily small constant. But it was additionally shown there that this only happens in what are, at least for applications, somewhat special cases – the knot must have regions where it is long and thin, in the sense that one strand can wrap around another in such a way that their tangents are nearly parallel and they are arbitrarily close together over a long distance. Such conformations cannot be constructed if the filament has non-zero thickness (as is the case with most real-world filaments). In the same work it was shown that the entanglement is bounded by the product of the curvature and the ropelength, where the ropelength is the ratio of the length to the radius of the thickest rope (the thickest tube with no self-intersections) one can place about the conformation (use the knot curve as the centerline of the tube)[3][2].

If we pack a C^2 curve of length l into a ball of radius r , then the total curvature K is such that $K \geq (l/r) - 2$. This is a lower bound – it is how much the string is forced to curve to fit into the ball: certainly it could curve more.[6] We also note that this result requires a continuous string – one could cut the string into small bits and pack it into the ball with no curvature at all. If we assume unit thickness for the filament, and pack it as tightly as possible into the sphere, then we will have a sphere of radius $r \approx l^{1/3}$, so by the above K is at least $K \approx \frac{l}{l^{1/3}} = l^{2/3}$. But we have shown that in this case entanglement is bounded by $l^{4/3}$, so we have that entanglement is bounded by K^2 [2][4]. Note that one usually cannot find lower bounds for entanglement – because it is usually possible to make a conformation with no essential crossings (the unknot). We have developed, however, a theory of expected entanglement[4], and we have in general that for a long string the expected entanglement is bounded by K^2 . This bound is not generally sharp: consider a string of trefoils tied in a rope. In this case both the curvature and the entanglement grow linearly with the number of knots in the rope. So it remains to generally characterize the relationship between curvature and entanglement. Numerical modelers have studied the total curvature of models of stochastic filaments, providing growth estimates for specific models of long strings[16].

We would like to focus on the effect of curvature on entanglement by considering the basic practical question above: given that we need to pack a certain amount of length in a certain volume, how should we manage the bending, the curvature, so as to minimize entanglement? So, we fix the density (the length per volume), and ask: how does entanglement tend to vary as we vary curvature?

We can do this analysis in the following model system. Let circles be centered at each lattice point in the cubic lattice (three dimensions) for some finite cube of fixed size, where the cube is large enough to contain many lattice points. Let the circles be randomly oriented with respect to one another. (A similar analysis could likely also be done for circles with randomly placed centers and random orientation). We will vary this system by changing the number of circles, that is, the distance between the lattice points, while keeping the total length constant – so we have to vary the radii of the circles as we vary the lattice spacing. The idea is that this way we are keeping the density constant – since it is just the length per unit volume, but varying the curvature, since the total curvature is simply $2\Pi N$, where N is the number of circles. Let us say that the total length is L . Then the length of each circle is $\frac{L}{N}$, so the radii are $\frac{L}{2\Pi N}$. There are N circles in the cube, so the distance between the centers of nearest neighbors is $N^{-\frac{1}{3}}$ (assuming a cube of width 1).

This system, for various N , is depicted in Figure 1. A system of randomly placed circles with the possibility of linking has been used to model mitochondrial DNA from trypanosomes[8].

Now, how to measure the entanglement? In this system there is one straightforward method: simply count how many pairs of circles are linked. For an estimate, we will simply assume that some percentage of circles which could be linked are, that is, the pairs of circles whose centers are closer to one another than twice the radii. To be more precise, the probability of linking of two circles as a function of the distance between their centers has been studied [10][9], and we could use a better approximation, but we will continue on this track for the nonce. So the question becomes: for a given circle, how many other circles have their centers within two radii? The radii are $\frac{L}{2\Pi N}$, so the question becomes, how many lattice points, where the lattice unit is $N^{-\frac{1}{3}}$, are in a ball of radius $\frac{L}{\Pi N}$? But this is approximately:

$$\frac{4}{3}\Pi \left[\frac{\frac{L}{2\Pi N}}{N^{-1/3}} \right]^3.$$

Now this is the estimate for the linking of a single circle. There are N circles, so our estimate for the entanglement is

$$\frac{4}{3}\Pi \left[\frac{\frac{L}{2\Pi N}}{N^{-1/3}} \right]^3 N = \frac{L^3}{6\Pi^2 N}.$$

This is order $\frac{1}{N}$ for a fixed length L . Since the total curvature is just $2\Pi N$, we have that for the regime where our assumptions are reasonable the entanglement as a function of the total curvature decreases with the inverse – the more the curvature, the less the entanglement.

In the limit of many, many circles, the estimate will fail because there will come a point where the radius is so small that even neighboring circles cannot be linked. This happens when $N^{2/3} > L/\Pi$. $N^{2/3} = L/\Pi$ gives an estimate of order N , which is the point when each circle only links with its nearest neighbors – a bit more distance between circles and this last connection is lost. If we were to proceed in the other direction – decreasing the number of circles, we reach the point where the radius of the circles is on the order of the size of the cube, and so we can no longer assume that the number of circles with centers within two radii grows with the radii (the circles become larger than the box). The assumption in this limit is that each circle links with a percentage of all of the other circles, and so the estimate is order N^2 , and the entanglement limit here would also be 0, reached when the number of circles is 1.

In Figure 2 we can see the shape of the graph that gives entanglement as a function of total curvature, keeping density constant. Beginning from small total curvature (few circles) to large total curvature (many circles), we have a graph that increases to a maximum, then declines with an inverse tail, and the tail transitions to become identically zero at some finite point. This graph is intended only as a qualitative description, no particular modelling function is implied.

In [17] the authors discussed a model of DNA packed in phage heads. The idea was to learn something about the packing geometry by studying knots created by the geometry. They found (among other things) that increasing the stiffness of the DNA led to an increase in knot formation (the length of the DNA is kept constant, as is the volume of the phage head, so the density is constant). This is in keeping with the analysis we have presented here. Increasing stiffness tends to decrease curvature, so the finding in this case is that a decrease in curvature led to an increase in entanglement. So the implication is that the model under study is in the regime past the entanglement maximum, where increasing curvature decreases entanglement (they are simply moving in the opposite direction as compared to our presentation – decreasing curvature instead of increasing it).

In Figure 3 we have a two dimensional schematic representation of the relationship between curvature and entanglement. Here in the top row we have circles arranged in a plane in two dimensional grid inside a box. Each box is the same size (9 by 9), and the total arc-length is the same (36Π). We simply use the number of crossings as a proxy for entanglement, and the total curvature is $2\Pi N$, where N is the number of circles. In the left frame there are 4 circles and 12 crossings. In the middle frame there are 9 circles and 24 crossings. In the right frame there are 16 circles and 0 crossings. In the second row we have a similar schematic with a single continuous curve in each frame. We have numerical estimates of the arclength and the curvature in each frame, note that the arclength is nearly constant across the three frames. The box size is 2 by 2 in each frame. In the left frame the arclength is approximately 21.0468, the curvature is approximately 25.1327, and there are 15 crossings. In the middle frame the arclength is approximately 21.0456, the curvature is approximately 69.115, and there are 36 crossings. In the right frame the arclength is approximately 21.0418, the curvature is approximately 119.381, and there are 20 crossings. In the third row we see examples of straight, wavy, and curly hair, at approximately the same scale. This is for illustration only – we do not have experimental data on human hair

entanglement, but the general principle elucidated in this paper predicts that at some level of curliness entanglement as a function of length (with constant density) would begin to decline.

We can use this analysis to get some sense of the benefit of coiling in the avoidance of entanglement. DNA is supercoiled in many circumstances[18][19][20], and the approach here could perhaps be thought of as a conceptual guide for that application, we offer an approach to the simple coil often seen in telephone cords and other filamentary objects in everyday use. We ask: say we took the circle system discussed here, and turned the circles into circles of coils, would this increase or decrease entanglement? As before, we preserve total length and volume, so as the length is taken up by the coiling, we reduce the number of circles. Our new object is roughly depicted in Figure 4. Say the coil radius is $1/10$ the radius of the original circle. Say there are 20 coils in a full transit of the object. Then the new length is roughly the original length l plus 20 circles of length $l/10$, or $3l$. This is in keeping with experience – that a telephone cord can stretch to thrice its coiled length. But since we are keeping total length fixed, we now have $N/3$ circles. To estimate the entanglement of this system (in the middle regime above), we assume that it comes from two contributions – the more global interactions of the coiled loops with one another, and the more local interactions of the coils along a single loop. For the global interactions we have that the large radii are unchanged at $\frac{L}{2\Pi N}$, the grid unit has now become $\frac{3}{N^{1/3}}$ and so we get $1/9 \frac{L^3}{6\Pi^2 N}$. For local contribution we assume that the coils can only interact with near neighbor coils, so we get $N/3 \times 20$. (We can estimate the curvature of the coiled loop system as the number of loops plus the number of coils, or $\frac{21N}{3}$). So, if

$$1/9 \frac{L^3}{6\Pi^2 N} + \frac{20N}{3} < \frac{L^3}{6\Pi^2 N},$$

then this coiling inhibits entanglement. Note that this is not the case in the large N limit. Here coiling is counterproductive – the induced local entanglement from coiling outweighs the savings in larger loop entanglement. In fact coiling may not reduce entanglement for any N if L is small enough – coiling saves on entanglement in the reasonably dense regime. On the other hand, for high density there is a fairly wide range of parameter values for which coiling seems to be a very effective strategy for reducing entanglement. The transition from the second frame to the third frame of the middle row of Figure 3 can also be thought of as an illustration of this.

REFERENCES

- [1] J Bohr and KW Olsen. Total positive curvature of circular dna. *Physical Review E*, 2013.
- [2] Gregory Buck. Four-thirds power law for knots and links. *Nature*, 392(6673):238–239, 1998.
- [3] Gregory Buck and Jeremy Orloff. A simple energy function for knots. *Topology and its Applications*, 61(3):205–214, 1995.
- [4] Gregory Buck and Jonathan Simon. The spectrum of filament entanglement complexity and an entanglement phase transition. *Proceedings of the Royal Society A: Mathematical, Physical and Engineering Science*, 468(2148):4024–4040, 2012.
- [5] Gregory R Buck and E Lynn Zechiedrich. Dna disentangling by type-2 topoisomerases. *Journal of molecular biology*, 340(5):933–939, 2004.

- [6] Gregory R Buck and Jonathan K Simon. Total curvature and packing of knots. *Topology and its Applications*, 154(1):192–204, 2007.
- [7] Richard W Deibler, Jennifer K Mann, L Sumners De Witt, and Lynn Zechiedrich. Hin-mediated dna knotting and recombining promote replicon dysfunction and mutation. *BMC molecular biology*, 8(1):44, 2007.
- [8] Y Diao, K Hinson, R Kaplan, M Vazquez, and J Arsuaga. The effects of density on the topological structure of the mitochondrial dna from trypanosomes. *Journal of mathematical biology*, 64(6):1087–1108, 2012.
- [9] Y Diao and EJ Janse van Rensburg. Percolation of linked circles. In *Topology and geometry in polymer science*, pages 79–88. Springer, 1998.
- [10] Yuanan Diao. Unsplittability of random links. *Journal of Knot Theory and its Ramifications*, 3(03):379–389, 1994.
- [11] Hendrik Dietz, Shawn M Douglas, and William M Shih. Folding dna into twisted and curved nanoscale shapes. *Science*, 325(5941):725–730, 2009.
- [12] Lance E Edens, James A Brozik, and David J Keller. Coarse-grained model dna: Structure, sequences, stems, circles, hairpins. *The Journal of Physical Chemistry B*, 116(51):14735–14743, 2012.
- [13] Ashley H Hardin, Susanta K Sarkar, Yeonee Seol, Grace F Liou, Neil Osheroff, and Keir C Neuman. Direct measurement of dna bending by type iia topoisomerases: implications for non-equilibrium topology simplification. *Nucleic acids research*, 39(13):5729–5743, 2011.
- [14] Michael A Lomholt, Bram van den Broek, Svenja-Marei J Kalisch, Gijs JL Wuite, and Ralf Metzler. Facilitated diffusion with dna coiling. *Proceedings of the National Academy of Sciences*, 106(20):8204–8208, 2009.
- [15] J.W. Milnor. On the total curvature of knots. *Annals of Mathematics*, 52:248–257, 1950.
- [16] Patrick Plunkett, Michael Piatek, Akos Dobay, John C Kern, Kenneth C Millett, Andrzej Stasiak, and Eric J Rawdon. Total curvature and total torsion of knotted polymers. *Macromolecules*, 40(10):3860–3867, 2007.
- [17] Daniel Reith, Peter Cifra, Andrzej Stasiak, and Peter Virnau. Effective stiffening of dna due to nematic ordering causes dna molecules packed in phage capsids to preferentially form torus knots. *Nucleic acids research*, 40(11):5129–5137, 2012.
- [18] JB Schwartzman, ML Martinez-Robles, P Hernandez, and DB Krimer. The benefit of dna supercoiling during replication. *Biochem Soc Trans*, 41(2):646–651, 2013.
- [19] Bram van den Broek, Michael Andersen Lomholt, S-MJ Kalisch, Ralf Metzler, and Gijs JL Wuite. How dna coiling enhances target localization by proteins. *Proceedings of the National Academy of Sciences*, 105(41):15738–15742, 2008.
- [20] Guillaume Witz and Andrzej Stasiak. Dna supercoiling and its role in dna decatenation and unknotting. *Nucleic acids research*, 38(7):2119–2133, 2010.

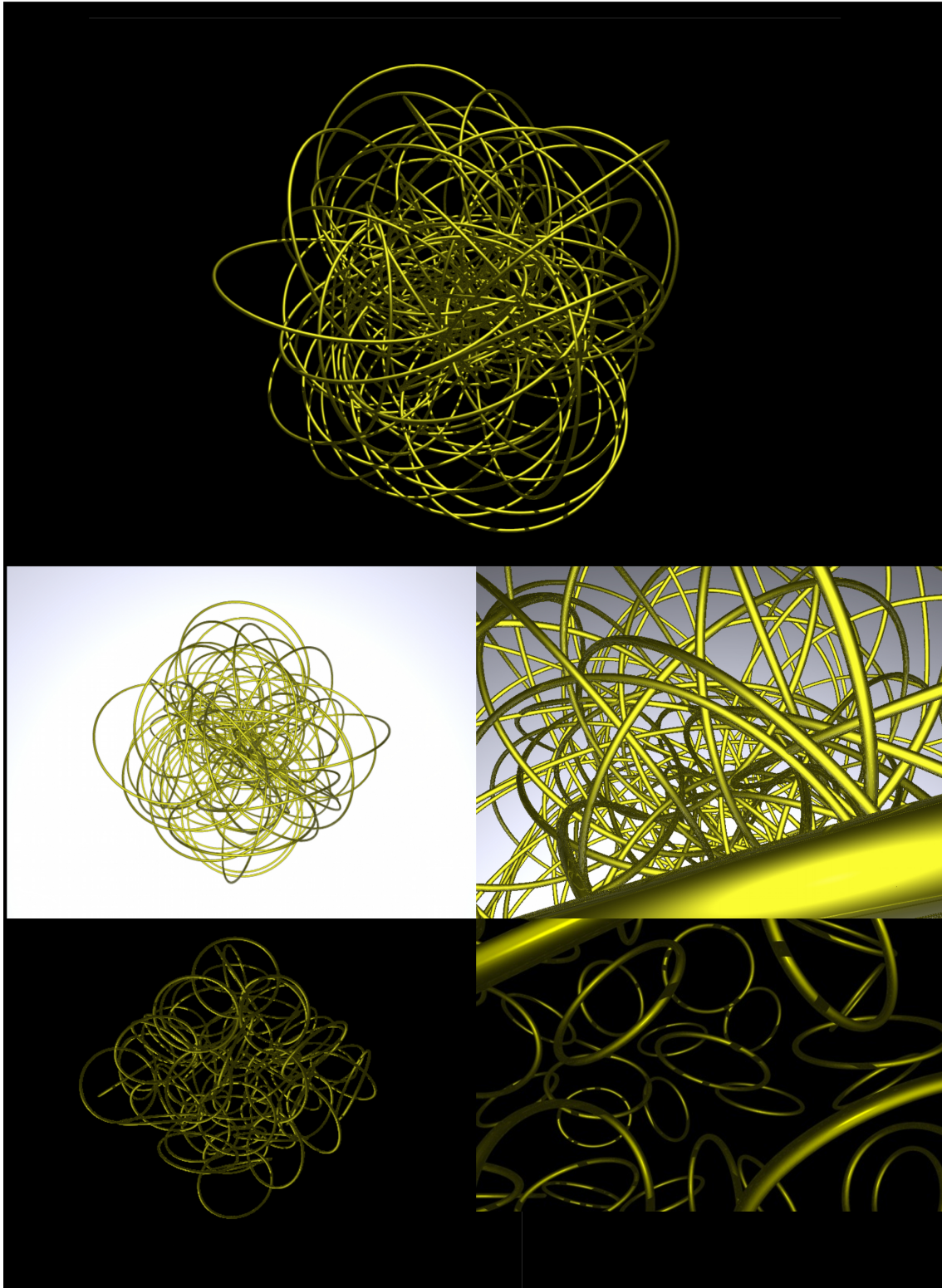


FIGURE 1

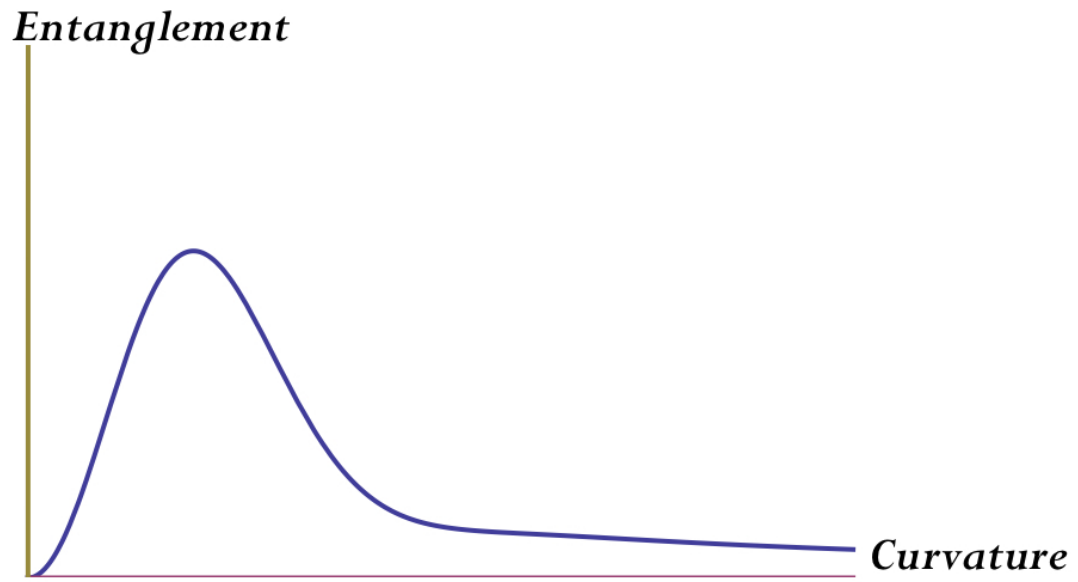


FIGURE 2

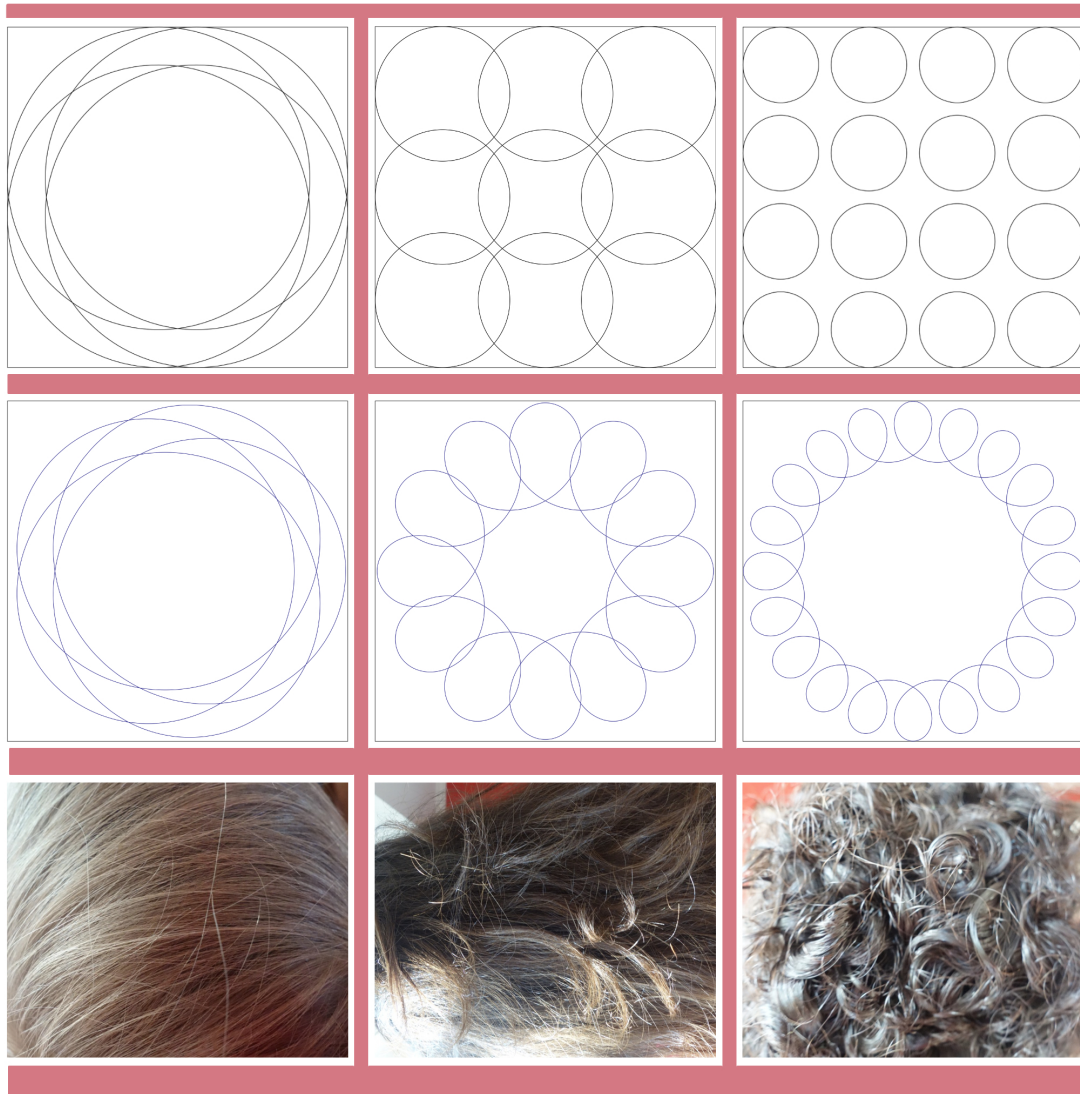


FIGURE 3



FIGURE 4