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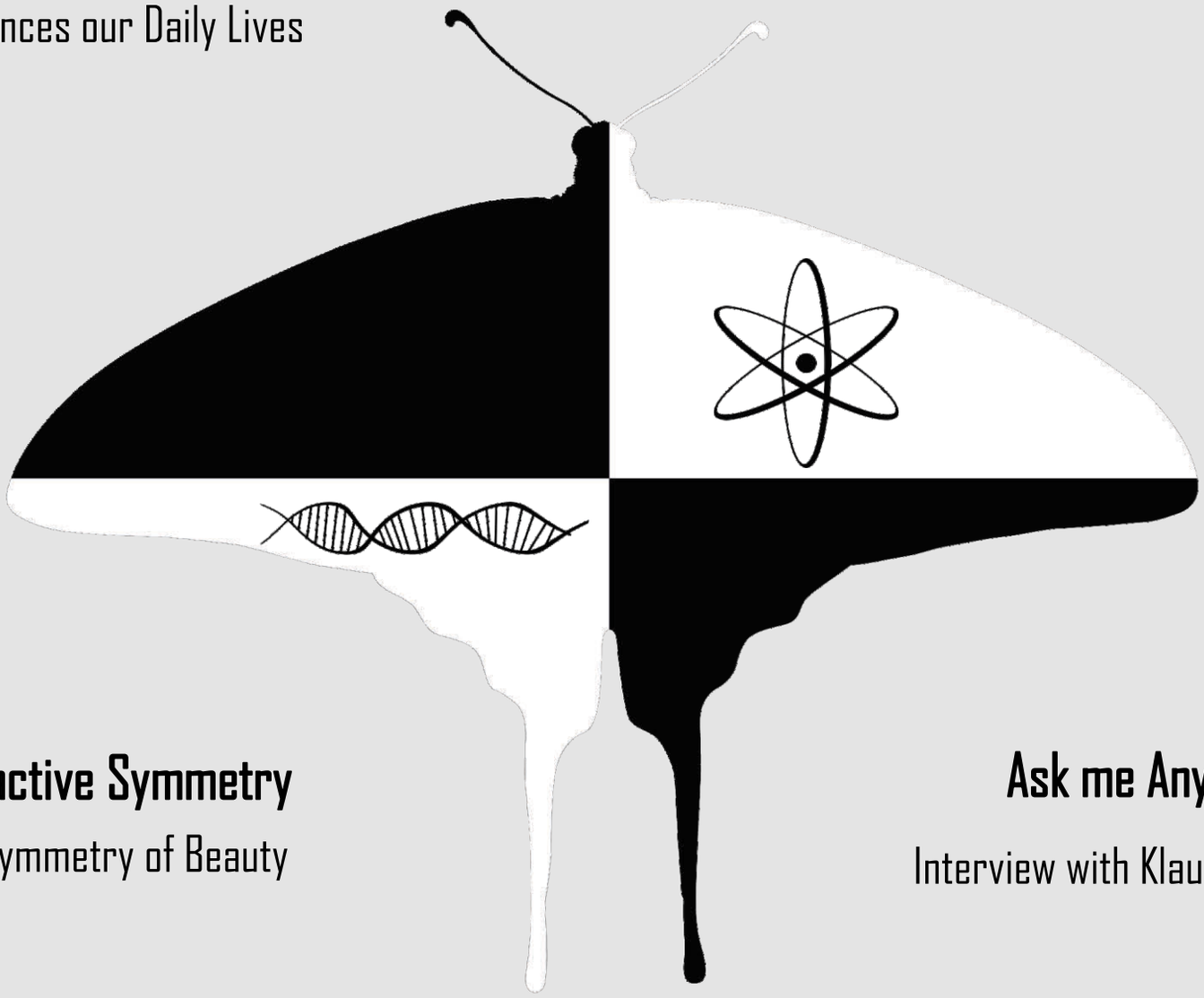
Winding Wonderland

How Symmetry in Chemistry Influences our Daily Lives

Bats, Masks, and Dancers

A short Glimpse at the Rohrschach Test



Attractive Symmetry

The Symmetry of Beauty

Ask me Anything

Interview with Klaus Roth

SYMMETRY IN SCIENCE

SYMMETRY IN SCIENCE

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Preface

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"The universe is built on a plan and the profound symmetry of which is somehow present in the inner structure of our intellect."

Paul Valery

Dear Reader,

Symmetry is a striking concept that is encountered everywhere in nature, science and art. It is said to be perfect, harmonic and tidy. Throughout history, architects and artists have put great stress on symmetric features of their work. Symmetric faces are said to be most beautiful. Is it true or a mere misconception? Read more in our article "Attractive Symmetry" on page 1. The way we perceive symmetric objects or images apparently tells us something about our state of mind. Hermann Rorschach believed that inkblots expose psychological conditions and paved the way to a controversially discussed method in psychoanalysis: Klecksography. Read more on page 5. Symmetry even affects our health and physical state, from macroscopic sensations to biochemical reactions on the nanoscale. Learn more about the role of "Symmetry in Chemistry" on page 9.

In November '19, we were honored by Klaus Roth who, once more, held a talk in Mainz with the title "Die Chemie des Katers" (loosely translated: "The Chemistry of the Hangover"). In an "ask-me-anything" interview on page 14 we get to know him a little better.

We had to postpone the publication of this issue a little due to the CoVID-19 outbreak. We hope to soothe your life a little with our humble contribution. Stay healthy and dig through the JUnQ to find the hidden treasures!

— Tatjana Daenzer

Opinions

Attractive symmetry

Mariia Filianina, Tobias Ruff

Symmetry in natural sciences like mathematics and physics is understood very precisely. An object is said to be symmetrical if it is invariant under certain transformations. However, generally, coming from Greek, the word "symmetry" implies "agreement in dimensions, due proportion, arrangement".[1] Whether symmetry is beautiful has always been a very controversial topic.

On the one hand, symmetry as proportion and balance in a dimensional sense has always been present, for example, in architecture though out all times starting from ancient Greek temples and pantheons. We can find symmetry not only in the outside view of the buildings but also in the layout of the individual floor plans, and even in the design of constituent building elements. In ancient Greece, people thought that everything in nature was balanced or symmetrical in a certain way. Thus, the buildings were designed to copy the proportions and lines of symmetry as they were seen in the world around. Looking, for example, at the ancient Pantheon of Athens, don't we still find this building appealing even after so many years?

Figure 1: Parthenon illustration, published in 1688, depicting the structure in its entirety, by Vincenzo Coronelli.

On the other hand, symmetry is often regarded as static and is therefore perceived boring. This was discussed by William Hogarth in the book "The analysis of beauty",[2] who casted doubts on the conventional appreciation of symmetry's contribution to beauty. According to Hogarth, exploring fundamental principles that bestow elegance and beauty, variation within uniformity is key. Among other ideas of beauty, Hogarth introduced the concept of the "line of beauty".

This term refers to an "S"-shaped curve, which, according to Hodarth, signifies liveliness and excite the attention of the viewer as contrasted with straight lines. This is sort of a secret hack of creating beautiful things most people do not know about.[3]

The middle ground of this debate would be to say that symmetry is at least attractive. Indeed, a recent study shows that the more symmetrical a human body is, the more it appears appealing to other humans independently of their sex.[4] Using a 3D optical scanner Brown *et al.* explored topographies of 77 human bodies, the length of their arms, legs and their proportions, and finally evaluated them based on the degree of bilateral symmetry, i.e., the symmetry between the left and the right sides of the bodies. Then, 87 volunteers were asked to rate the attractiveness of these 3D models, which revealed the correlation between the bodily symmetry and how highly rated the person was by others.

Furthermore, earlier studies show that also facial symmetry has a positive influence on facial attractiveness rating.[5] Evolutionary scientist Lisa DeBruine and psychologist Ben Jones who run a so-called Face Research laboratory (http://faceresearch.org/demos/average), which contains interactives and online experiments that analyze how we process faces, demonstrate that, upon adding faces and taking the average of their features, the composite generally is more attractive than any individual face.[6] Explore their interactive to see how the more faces you "add", the more attractive a new face becomes. Adding only two faces is not necessarily better than one, but once you get up to five or six, the composite consistently becomes more attractive.

Figure 2: The line of beauty denoted on Hogarth's Beer Street sign painter.

The explanation to this striking result is that during blending humans' faces one averages the averageness of the individual faces. And what one gets at the end is a highly symmetrical face which, as discussed earlier, is likely to be appealing.[7,8]

However, the correlation between facial symmetry and physical attractiveness is controversial: By avoiding averaging of faces when rendering images of them more symmetrical, Swaddle and Cuthill found a positive relationship between asymmetry and perceived attractiveness.[9] They speculate that this could be due to average faces appearing less emotional.

Now, why humans are so sensitive to symmetry is particularly interesting, because in most cases, the differences between the left and right sides of our bodies are as small as 1-3%.[10] What makes us able to pick up these subtle differences and what is the reason for this?

The most dominant theory is that bodily or facial symmetry implies uniform development and is, therefore, a quick visual marker for good health.[8,11,12] During the development process of a meant-to-be symmetric creature, if the developmental gene expression worked perfectly, the result would be perfectly symmetric. Therefore, anything less than a perfect symmetry may indicate that something went wrong. This happens when some genes are expressed too strongly or too weakly on one side of the body, or at a slightly wrong place, or a little earlier or later, the resulting tissue will look slightly different from the other. Most of these small malfunctions are tiny and lead to what is called fluctuating asymmetry. The degree of this asymmetry is believed to be an indicator of poor development and as a consequence that the individual is less adapted to the environment and more likely to produce fewer off-spring etc. Therefore, the perfectly symmetric bodies are, in a sense, testament to the quality of their owners as mates.

An interesting study shows that people with more symmetrical faces are better dancers.[13] Using a motion camera, over a hundred dancing people were filmed, and their movements were transferred onto impersonal characters, which were then evaluated by participants of the opposite gender. The outcome of this study suggests that higher body symmetry may also indicate better neuromuscular coordination, which supports that a high degree of bodily symmetry is generally related to genetic quality.

As we know, most people do not go around with a scale and measure body parts of potential mates. Nature took care of this too. Perhaps, because we ourselves are bilaterally symmetric, we can pick up these subtle asymmetries in other humans, not necessarily consciously. Astonishingly, babies at 2 months of age already prefer to look at more symmetrical faces, as it was shown in a recent study.[14] This also supports the hypothesis that our preference for symmetry is built-in and the ability to sense it is a result of evolutionary development. Note that a similar bias for symmetry is observed in animals as well.[15]

To conclude the discussion about why humans are drawn to symmetry in other humans, we repeat that the general interpretation is that symmetry is a marker of health. Now, whenever you get a question "What is your best side", the ideal answer would be "Both".

A practical conclusion to this discussion is that it is also possible to trick our symmetry perception thanks to so-called "beer google" phenomenon: "Beauty is in the eye of a *beerholder*".[15] A number of studies shows that alcohol impairs our ability to perceive asymmetry, and this could potentially be the reason for people appearing more attractive when we are under the influence.[16] Even more intriguing is that the alcohol, in this case, is not strictly

necessary, people just need to *think* they drank some.

Read more:

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Bats, Masks, and Dancers - A Short Glimpse at the Rorschach Test

Tatjana Dänzer

Klecksographies (from the German word *Klecks* meaning spot or blot), or simply called inkblots, were commonly used in the 1800s as illustrations and games for children. Their meaning for psychological research has been already independently emphasized by psychologists and physicians like Szymon Hens, Howard Andrew Knox, and Justinius Kerner.[1-3] The swiss psychologist Hermann Rorschach (1884-1921) was the first to systematically explore the influence of optical input, especially inkblots, to the subconsciousness of his subjects.[4]

Figure 1: Hermann Rorschach at the age of 26.[5] (public domain - wikimedia commons).

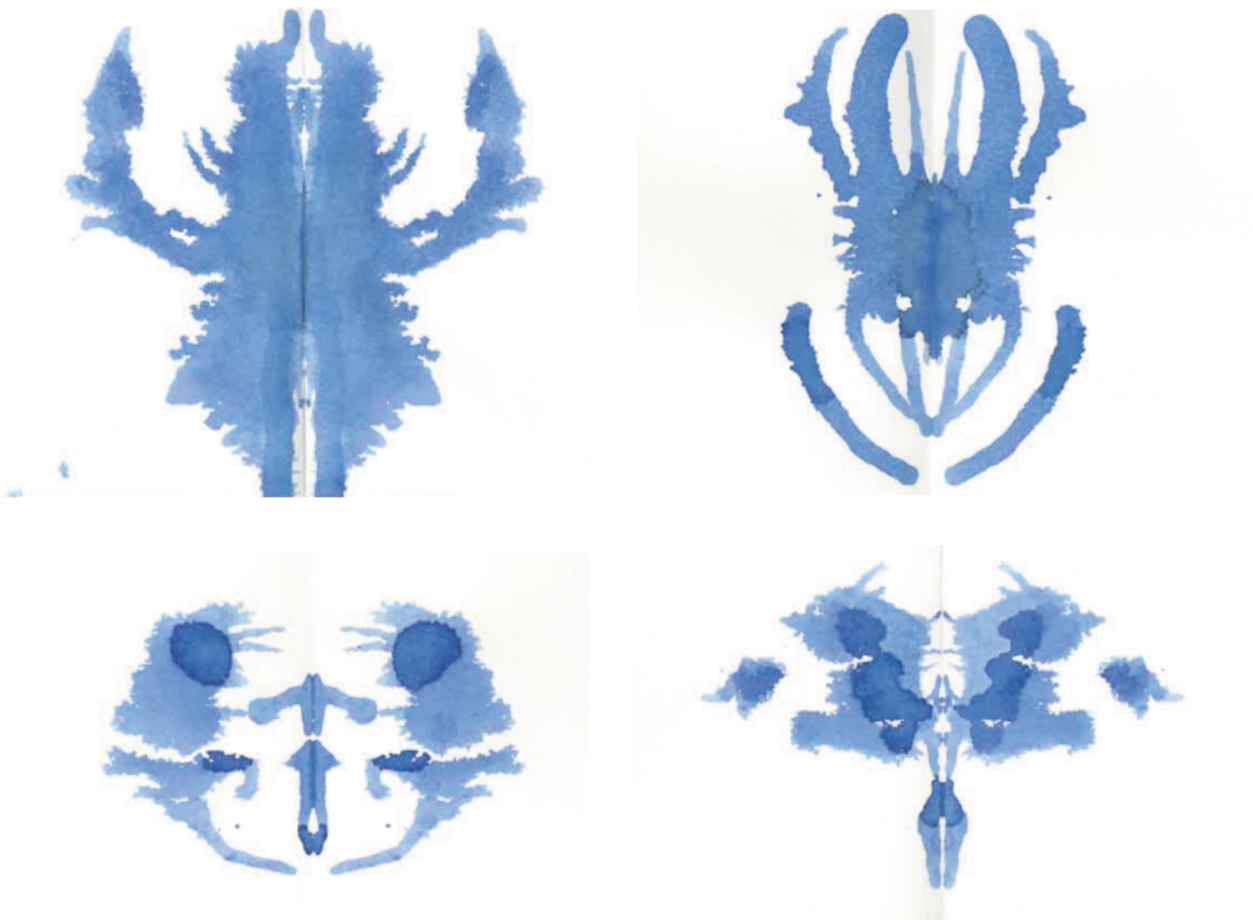
The effect that is triggered by such images is called "apophenia" which is the inclination to read a higher meaning into a meaningless image or pattern. It is not necessarily a critical psychological condition as most humans tend to see familiar regular shapes in random patterns.[6] Rorschach experimented with a variety of inkblots and finally chose symmetric blots.[7]

"Asymmetric figures are rejected by many subjects; symmetry supplied part of the necessary artistic composition. It has a disadvantage in that it tends to make answers somewhat stereotyped. On the other hand, symmetry makes conditions the same for right and left-handed subjects; furthermore, it facilitates interpretation for certain blocked subjects. Finally, symmetry makes possible the interpretation of whole scenes."

In Rorschach's opinion, right and left-handed people scan the left and right side of an asymmetric object differently. To ensure equal evaluation of the subjects without regarding their handedness, he chose symmetric blots. Also, vertical symmetry is perceived as more pleasant than horizontal symmetry - perhaps because it reminds of natural objects like leaves or insects. Other theories suggest that symmetry is related to "social" oriented movements like dancing and kissing, while asymmetry is related to a "solitary" and unbalanced movement.[8]

Figure 2: Example of an inkblot as used in the Rorschach Test. The subjects usually see human or animalistic figures like dancers, angels, a wizard, a skull or mask, or a moth.[9] (public domain - wikimedia commons).

The creation of an inkblot is easy: a drop of ink is placed on a plain paper which is then folded in half. The ink spreads across the sheets and forms a blot with a random shape. In some cases, multiple colors are used, or some details are added by hand. In conversation with a psychologist, the subjects discuss their responses and emotions that were evoked by the different shapes and colors. The time the subjects need for a response, the way they perceive and interpret the content, and how they express their responses give hints on their state of mind, character and relationships.[10] The blot in the image above, for example, is often perceived as a bat or butterfly. Fixation on dark colors and shades or the perception of male and female body parts were often considered to be subject to depression, sexual preferences, or the relationship to parents and partners.[11] In Rorschach's time, this method was a promising approach to literally draw a picture of someone's mind. The perception and response to the Rorschach Test is, of course, subject to differences in age and culture. In addition, the inkblot evaluations are prone to error and false interpretation. The conclusions that were drawn by different psychologists in the first half of the 20th century from the same subject often differed tremendously and severe misdiagnoses have been made. In some studies, it was not possible to distinguish



between healthy aviation students and psychoneurotic patients or between creative writers and mathematicians.[12-14] Not to mention those subjects who were wrongly diagnosed with homosexuality.[15]

Modern evaluation, however, is far more complex than its superficial and even somewhat subjective precursor. The Holtzman inkblot technique is one attempt to grade the responses of the subjects. It is an improvement to the Rorschach Test since it consists of a considerably larger number of inkblots and the responses are scored by 22 variables which enable a quantitative assessment of the subjects.[16] Another prominent method is the Exner Scoring System that works with clusters of variables.[17] Inkblot tests are still famous in psychoanalytic studies and even forensic examinations, especially in the US.[18] In any case, modern psychoanalysis never relies solely on the Rorschach Test but on the findings of a series of examinations.

The photographer Mathieu Piranda takes the Rorschach Test to another level: he takes photos from landscapes and natural objects like trees or mountains and mirrors them along a vertical axis. In this way, he transforms his photos into a digital version of the Rorschach Test. His intentions are, of course, of an artistic rather than a psychoanalytic nature. But with his art, he raises questions about the naturalness of symmetry and the emotions that are triggered by looking at his photos.[19]

The official inkblots that are used in the Rorschach Tests today are not accessible publicly in order to not influence potential testees with possible answers. We took the liberty to create some inkblots on our own. Take a look, test your imagination, and don't get too "psyched".

Read more:

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Winding Wonderland: How Symmetry in Chemistry Influences our Daily Lives

Tatjana Dänzer

By sketching molecules on a plain paper, we immediately get the impression that chemistry is a two dimensional and flat world. But the versatile chemical nature of the building blocks (i. e. the atoms) enables a wide variety of geometries that can occur in the molecules. The symmetry of chemical structures is of high importance for their properties. This is especially significant in organic and pharmaceutical chemistry. The most important feature of such molecules is a stereogenic or chiral center that causes a variety of molecules with different physical configurations called enantiomers.

Figure 1: Left and right hands are chiral.[1]

The most prominent examples for enantiomers are our hands (or feet): the right hand mirrors the left hand and vice versa but they will never align when facing the same direction. The very same applies to molecules. The upper part of Fig. 2 shows the so-called Natta projection of an exemplary molecule consisting of a carbon center with four different substituents A-C with decreasing valency. By switching the positions of two substituents (e. g. A and B) we obtain a molecule that mirrors the original version but is not the same. The configuration of the molecule can be described following the rules of Cahn, Ingold, and Prelog:[2] the substituent with the lowest valency - in our example D - points towards the back while we look at the molecule from above, like on top of an umbrella (lower part of Fig. 2). If the valency of the three remaining substituents is decreasing in the clockwise direction, the molecule is called *R* enantiomer. If the valency is decreasing counterclockwise, the molecule is called *S* enantiomer. The synthetic circumstances define the enantiomer of a certain chemical substance. In real organic molecules, the substituent with the lowest valency is most often just a proton and is thus not shown in the two-dimensional projection for simplification (right side in the lower part of Fig. 2). In pharmaceutical chemistry, the active enantiomer is called eutomer, while the inactive enantiomer is called distomer.

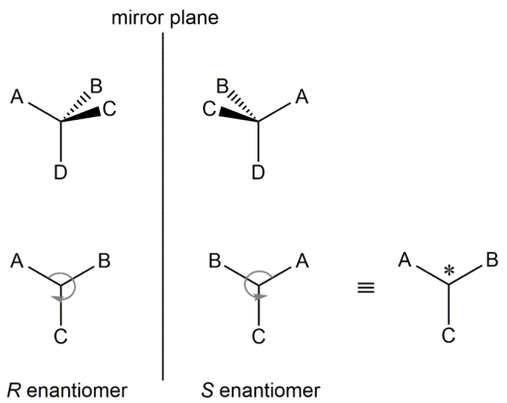

Figure 2: Like our left and right hands, chiral molecules will never align. The two enantiomers of such a molecule with a carbon atom that bears four different substituents with decreasing valency from A to D are shown on the right side. The bold bond indicates that the functional group is pointing out of the paper, while the dashed line indicates that the functional group lies in the back of the paper plane. The chiral center in a molecule is usually indicated by an asterisk.

Although it is mostly unnoticed, chiral molecules are permanently present in our daily lives. Enantiopure substances interact directly with light, meaning that a linear polarized beam of light is rotated either clockwise (denoted "levorotatory", "-" or "L") or counterclockwise (denoted "dextrorotatory", "+" or "D"). This is called optical activity. A mixture that contains equal parts of the *R* and *S* enantiomers is called a racemate and is not optically active. This can be of use for Liquid Crystal Displays (LDCs).

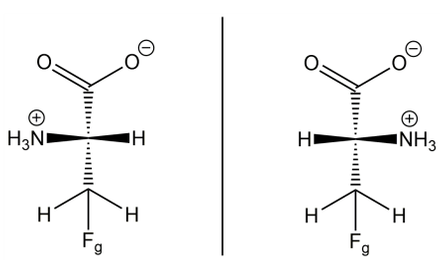

Figure 3: The two enantiomers of an amino acid. The L-enantiomer is on the left side, the D-enantiomer is shown on the right side. F_g is the functional group that defines the amino acid.

But the role of chiral molecules is much more vital to us. Without amino acids - the building blocks of proteins - life as we know couldn't exist. There are 20 naturally occurring proteinogenic amino acids that are responsible for the translation processes of the genes. Of those 20 amino acids, only one is *not* chiral.[3] Figure 3 shows the general structure of amino acids in the so-called Fisher projection. By convention, the carboxylic acid is on top while the carbon with

the lowest oxidation state is on the bottom of the molecule chain. Depending on the enantiomer, the amino group is either on the left side (L) or the right side (D).

For the building of proteins, L-amino acids are essential. Their configuration contributes to the packing of the protein chains. The D-amino acids, on the other hand, are less common but not unnatural. They are, for example, formed through UV-B irradiation of the L-enantiomers.[4]

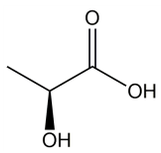

Figure 4: L-lactic acid ((R)-2-Hydroxypropanoic acid).

In the dairy aisle of the supermarkets you might be confronted with yogurt that is advertised with a high content of right-handed cultures. This does not mean that the bacteria that are responsible for the fermentation process have a favored direction of stirring rotation. It refers to the ability of the used starter cultures to produce more L- or *S*-lactic acid, as shown in Fig. 4. For people with a rather sensitive digestive system, L-lactic acid (which is right-handed because polarized light is rotated to the right side) might be easier to digest.[5]

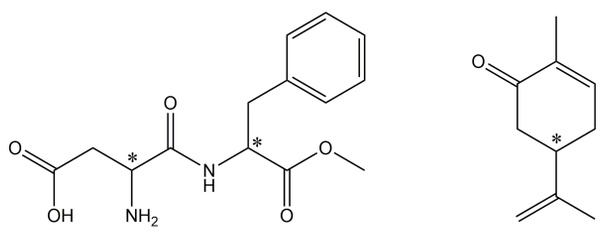

Figure 5: Left side: aspartame ((S,S)-N-(α-Aspartyl)-phenylalanine 1-methyl ester). Right side: carvone ((RS)-2-Methyl-5-(prop-1-en-2-yl)cyclohex-2-en-1-one).

In some cases, we can even smell or taste the different enantiomers: the common artificial sweetener aspartame (left structure in Fig. 5), which has two chiral centers, is only sweeter than sugar in its *S,S* configuration (D-aspartame). The *R,R, R,S,* and *S,R* enantiomers are tasteless. The reason is the enantioselective binding of the molecule on receptors for sweet taste, but the mechanism is not yet fully understood.[6] The naturally occurring carvone on the other hand, (right structure in Fig. 5), smells like mint in the *R* form and like caraway in the *S* form.[7]

As already implied above, the role of chirality in medicines and drugs is much more drastic. The following section gives an overview of some of the most prominent and important agents with a chiral center.

When in the 1950s thalidomide (shown in figure 6) was available over the counter in several European countries under the names Contergan and Softenon, many pregnant women were relieved from their heavy morning sickness and insomnia. As a tragic side effect, thousands of children suffered from dysmelia (severe deformities of the body caused by disruption of the embryo's development) depending on the state of pregnancy at which the drug was taken. In 1961, the drug was withdrawn. Present administrations of thalidomide are under strict surveillance.[8] Interestingly, only (S)-thalidomide is teratogenic while (R)-thalidomide is a potent sedative. But due to the acidic hydrogen which is located at the chiral center, racemization (that is the conversion of an enantiopure substance to the mixture) can occur even *in vivo*, making the administration of the pure R enantiomer useless.[9,10] Despite the teratogenicity, thalidomide is still listed among the WHO's list of essential medicines against multiple myeloma, a malignant disease of the plasma cells.[11] It is also suspected to be effective against leprosy.[12]

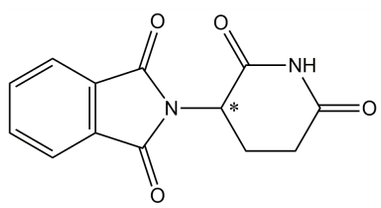

Figure 6: Thalidomide ((RS)-2-(2,6-Dioxopiperidin-3-yl)isoindol-1,3-dione.

To be able to control the motor function of the body, our nervous system needs neurotransmitters to send instructions from one cell to another. In the body, the eutomer levodopa or L-DOPA is produced from the amino acid tyrosine and acts as the precursor to many important neurotransmitters like dopamine and adrenaline. In contrast to dopamine, L-DOPA can pass the blood-brain barrier, which makes it a valuable prodrug for the treatment of Parkinson's disease for which necrosis of dopamine-producing nerve cells in the midbrain is characteristic. After passing the blood-brain barrier, L-DOPA is decarboxylated to dopamine, as shown in Fig. 7.[13] The distomer D-DOPA (the amino group points towards the back) is biologically inactive but can be converted into L-DOPA under certain conditions.[14] Dopamine itself acts as a precursor to L-adrenaline, which is needed for intuitive or visceral actions.[15] Like D-DOPA, D-adrenaline plays no role in the human body.

Quite similar is the effect of amphetamine and methadone (Fig. 8). Both are valuable drugs against depression or pain but, at the same time, often abused as drugs or doping agents. D- or *S*-amphetamine and L- or *R*-methadone are twice as potent as their respective enantiomers.[16,17]

Chirality is not necessarily exclusive to fully substituted carbon atom centers. The sulfur atom in pantoprazole bears three functional groups and a free ion pair that contributes to the steric configuration of the sulfoxide. Pantoprazol is a drug against heartburn and other gastro-intestinal diseases and is administered as a racemate.[18]

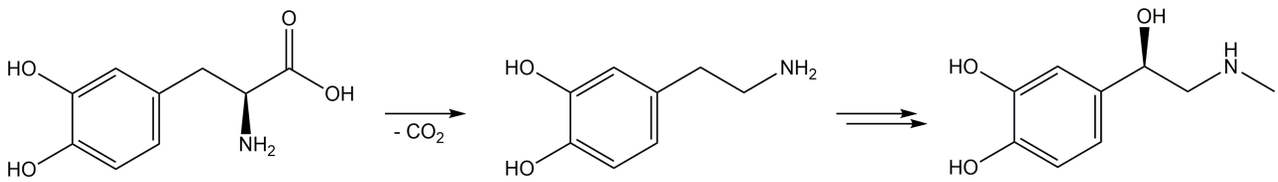

Figure 7: Decarboxylation of levodopa ((S)-2-Amino-3-(3,4-dihydroxyphenyl)propanoic acid)) to dopamine (4-(2-Aminoethyl)benzene-1,2-diole)) and further reaction to L-adrenaline ((R)-4-(1-Hydroxy-2-(methylamino)ethyl)benzene-1,2-diole).

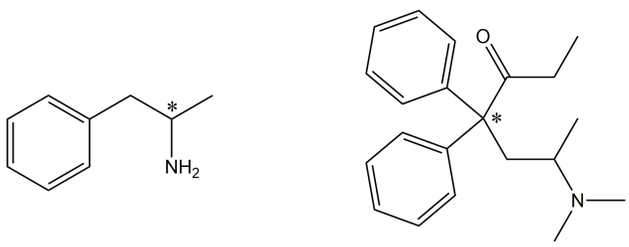

Figure 8: Left side: structure of amphetamine ((RS)-1-phenylpropan-2-amine). Right side: structure of methadone ((RS)-6-(dimethylamino)-4,4-diphenylheptan-3-one).

Finally, symmetry is not only bound to small molecules. The unraveled form of our DNA, for example, looks like a double helix, just like a corkscrew. Naturally occurring DNA is right-handed (D-DNA), meaning that the strands turn in clockwise direction as shown on the left side of Fig. 10. The biochemical mechanisms in our cells are precisely designed for this conformation. The enzymatic degradation of synthetic L-DNA, however, is much slower, which makes it a promising agent not only for biochemical applications but also as an asymmetric catalyst.[20,21]

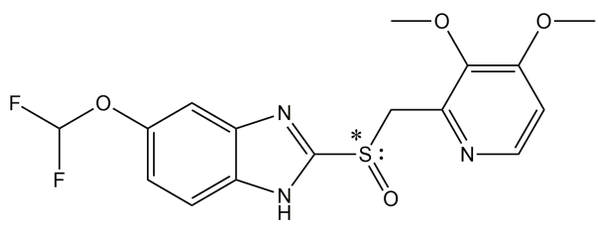

Figure 9: Structure of pantoprazole ((RS)-6-(Difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1H-benzo[d]imidazole).

A short strand of DNA or RNA called "aptamer" can trap and bind other molecules that are compatible. Figure 11 shows the example of an aptamer with a bonded small molecule, in this case, biotin. Aptamers that consist of L-oligonucleotides are called "Spiegelmers" and have already proven to be efficient binders for harmful proteins. Targeting of such proteins can decrease the death rate of patients significantly. C5a is such a protein and a known promotor for inflammations, sepsis and organ failure. Scientists from NOXXON Pharma AG in Berlin, Germany have developed a L-RNA/DNA aptamer called NOX-D20 that can selectively bind or trap C5a to inhibit its effect in mice and probably in humans. It is still in the test phase but shows already promising binding properties and increased survival rates of septic mice.[23]

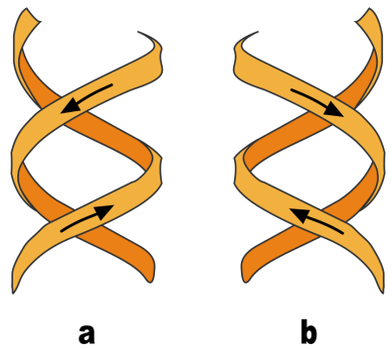

Figure 10: The two rotational directions of the DNA double helix (a = right-handed, b = left-handed).[19]

One last but important example of the role of chirality in our lives are polymers. A prominent example is polypropylene. It is commonly derived from propylene by heterogeneous catalysis, as indicated in Fig. 12. During the polymerization the methyl group contributes to the creation of a new chiral center. Depending on the catalyst, three different combinations of stereogenic centers along the chain can occur. This is called "tacticity". In an isotactic polymer, all

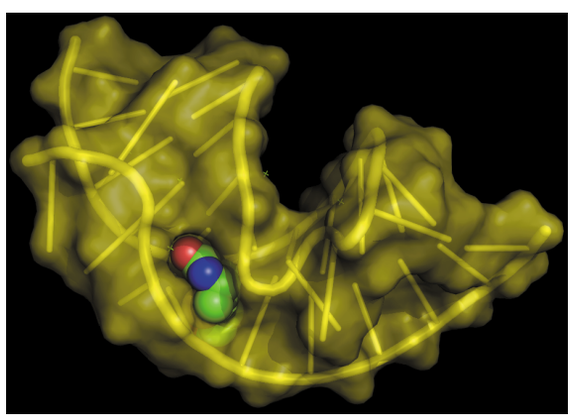

Figure 11: An aptamer (yellow) binds a small molecule in a suitable cavity.[22]

functional groups point towards the same direction, in a syndiotactic polymer, the groups point in alternate directions. Due to the symmetry, all polymer chains align optimally in the solid phase and the polymers can crystallize. In atactic polymers, the stereogenic centers are irregular and the polymer is amorph. This has a decreasing effect on meting points T_m and glass transition points T_g (below this temperature the polymer is brittle) from isotactic to atactic.[24] For your choice of material for certain applica-

tions, this knowledge is crucial.

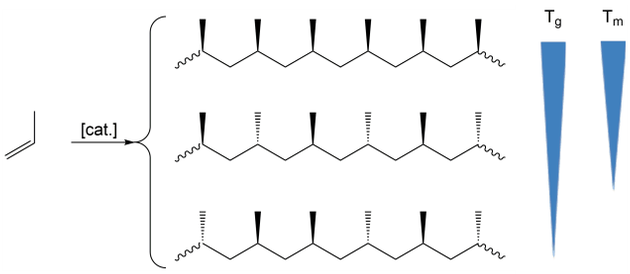

Figure 12: Different combinations of repeating chiral centers in the main chain of polypropylene. Top: isotactic, middle: syndiotactic, bottom; atactic. The tacticity affects the properties of the material like the melting point and the glass transition point.

Chiral polymers, for example, serve as packing material for various chromatographic methods that are needed for the enantioselective workup of racemic mixtures.[25] Through the choice of suitable monomers and side-chain modification even helical structures can be obtained. They can be ligands for ions or transition metals but are less relevant for the everyday world.[26]

Alas, the beauty of chirality is not easy to recognize to the untrained eye. Like our body with its pairs of hands, feet, eyes and so on, the nanoscopic world is full of mirror symmetry. The origin for homochirality in biologically relevant molecules is not yet found and may scientists suspect it to be found in the depths of space. But this is another story!

Read more:

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Prof. Klaus Roth

Freie Universität Berlin

„Chemie des Katers“

Do, 28.11.2019, 17 Uhr ct

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"Ask-Me-Anything" Interview with Klaus Roth

Klaus Roth[1] is an emeritus professor at the Freie Universität Berlin where he studied chemistry from 1964 – 1969 and completed his dissertation in 1973. After a post-doctoral stay at the Institute for Medical Research in Mill Hill, London from 1979 – 1980, he completed his habilitation at the Freie Universität Berlin in 1981. Between 1986 – 1988, he held a position as a visiting professor at the University of California in San Francisco, after which he returned to his home university as an extraordinary professor and became a full professor in 2000. During his research career, he dealt with many aspects of NMR spectroscopy but also popular science.

Klaus Roth publishes regularly in "Chemie in unserer Zeit" about the significance of chemistry in everyday life. You can find some of his articles on www.chemistryviews.org. On Nov. 28th, 2019 we invited him once again to have a talk at the university in Mainz about the chemistry of the hangover. For that occasion, students and researchers from our university were invited to send us questions from any kind of topic that we asked him together with the Young Chemists Form of Mainz in an "Ask-Me-Anything" interview. Here we present the "best-of" selection.

[1] klaus.roth@fu-berlin.de

JUnQ: Which value has symmetry in your life?

Klaus Roth: Some say symmetry is the mathematical form of beauty. But I counter with a saying from northern Germany "Beten scheef hett Gott leev!" which means "God likes it a little crooked". A little asymmetry can be charming. Of course, as an organic chemist, I had to deal with chirality and optical activity a lot.

JUnQ: What is your favorite molecule?

Klaus Roth: My favorite molecule is a chelate complex with an organic ligand, DTPA (diethylenetriaminepentaacetic acid), and a gadolinium center. It is used in nuclear resonance imagining as a contrast agent. It is not toxic and is injected intravenously in an amount of up to two grams. I have been involved in developments on this topic during my stay in San Francisco and together with the Schering AG.

JUnQ: Which historic moment in science would you like to have witnessed or even have been involved with?

Klaus Roth: Very hard to tell because there have been so many. You might find this strange, but I think very highly about the role of physics in the 1910s and 1920s. It practically turned the conception of the world and physics upside down once more every year. Just think of quantum mechanics and the discoveries of Max Planck and classic electrodynamics, that seemed to coexist incompatibly before. I guess these were exciting times!

JUnQ: Do you do any sports?

Klaus Roth: Since I am living in Berlin-Köpenick, getting in touch with soccer is inevitable (Union Berlin is my club!). I like doing sports myself and can't imagine living without it. I am a passionate tennis player, although I'm not very good.

JUnQ: How can we imagine the young Klaus Roth, and who were your role models?

Klaus Roth: Well, I'd say just like the old one. I think I kept my essential character traits and still feel young, at least mentally. I never had a particular role model, but I have always had lecturers from whom I have learned how to do it and also how not to do it.

JUnQ: Did you always want to be a chemist?

Klaus Roth: (laughs) When I was a kid, I wanted to be a pastry chef. Amazing job! I am mad about eating cakes. Making all those pastries and pies was a dream. Then I ended up being a chemist, which is nice too. Alas, you

can't eat what you have produced.

JUnQ: What is the most drastic experience from your student days?

Klaus Roth: I remember that I nearly failed because of one experiment in quantitative analytics training. It was the analysis of the separation of sodium and potassium, and I had to repeat it seven times because I never obtained the right results. And everyone else was faster. That is the most horrible memory that I have from my inorganic practicum. During the research on my diploma thesis, on the other hand, having the final product with the clean mass and NMR spectra in hand was a very uplifting moment, and I knew: this is my profession!

JUnQ: Which achievement in your life makes you most proud?

Klaus Roth: Being a father is the best thing I have achieved in my life. Everything else is not that important.

JUnQ: Imagine someone makes a movie about your life, who would play your part?

Klaus Roth: I cannot imagine that anyone would ever be interested in making a movie about that. But then, it absolutely must be George Clooney, of course.

JUnQ: With whom do you want to have a drink?

Klaus Roth: I guess it would be Hieronymus Bosch. He made some fantastic paintings, and I'd like to know where he got his inspiration from.

JUnQ: Which one of your talk topics is your favorite?

Klaus Roth: That's hard to tell because I like every one of them. Perhaps, what's most important to me has rarely been requested yet. It is the story of a young biochemist in Freiburg, Germany (in the 1930s), who's world drastically changed within half a year. He was first praised as a rising star and later in his life even became a Nobel prize winner. Then he was sort of expelled because of his Jewish ancestry and left the institute in a rush with just the words: "I need to catch the 11 o'clock train." His name was Hans Krebs, the co-discoverer of the citric acid cycle in England. After the war, he was the first one to take care of the reintegration of German scientists into the scientific community. An exceptional man! Unfortunately, this question did not yet attract much interest except in Freiburg.

JUnQ: How should our publication philosophy change, and how should the scientific community treat null and negative results?

Klaus Roth: Peer-reviewed journals should persist. Despite all the disadvantages and extra work that it implicates, it's the best we have. Of course, online access to information and journals is a vital improvement compared to the dull library research of the past. Today it's much more efficient. Negative results have always been neglected in the publications. But this is what *JUnQ* is trying to work against.

JUnQ: How do we approach more people outside of chemistry?

Klaus Roth: Chemists tend to think that they have a negative image in society. On the contrary, a research study from the Royal Chemical Society showed that we have a far better reputation. We are respected but don't recognize it. What people expect from us is more communication and clarification in a language that they understand. This is not taught by universities. I think every Ph.D. student should be able to describe their projects to their grandparents within two minutes in such a way that they say: "Gosh! You are doing an impressive job!". We need to train this because people are not ignorant per se. We simply should use an easier language to convey our passion.

JUnQ: How do we solve the problem of climate change?

Klaus Roth: It's not possible to answer this in just a few words. In any case, something must happen soon. It is, of course, reasonable to apply strict measures. But in the long term, the industry of a solitary country will decay or at least suffer. Without international cooperation and support from the Great Powers, it won't be possible. Right now, I'm very pessimistic, and I don't know what else must happen before everyone sits down at one table to talk.

JUnQ: Which food should we better not eat anymore?

Klaus Roth: In my opinion, food that you can buy in the supermarket, which is already processed and packed in aluminum, just to be fried or warmed up again – like roast potatoes, for example. It is no wonder that they contain preservatives. How else could they stay on the shelves for months? They are easy to make at home and taste much better. Those convenient foods should be evaluated by how much more sense it would make and money one would save by preparing them at home.

JUnQ: Imagine that Elon Musk invites you on a trip to the moon. Would you accept the invitation?

Klaus Roth: Now? Since I have seen the spatial conditions on those space crafts, I'd say most certainly not! Apart from that, the chemistry on the moon is definitively too inorganic.

But looking at our planet from so far away – I remember one picture from one of those voyager missions where the earth was just a tiny spot in the empty space – makes us appear to be much more irrelevant than we value ourselves.

I think people should be less occupied with themselves.

JUnQ: What is your favorite conspiracy theory?

Klaus Roth: Perhaps it is the anti-vaccination movement. To me, the whole discussion is incomprehensible. Just look at the statistics. It's a shame that the anti-vaxxers profit from those who take the vaccines. Nowadays, people don't consider hard facts anymore because their life has become too easy. They don't know what it means to be infected and seriously ill because most of us are vaccinated against whooping cough, rubella, smallpox, and so on. Nobody worries about their physical health anymore.

JUnQ: What's your best advice for young chemists at the beginning of their careers?

Klaus Roth: Most important: be well prepared for your job interview but be yourself. Read a newspaper daily, go to the theater, and try not to be a geek.

JUnQ: What's your universal message to every scientist in the world?

Klaus Roth: Peace and Cheers!

JUnQ: Thank you very much for the interview!
We would also like to thank the YCF team for their support!

— Tatjana Dänzer

Views on Life, the Universe, and Everything

Questions of the Month

The Journal of Unsolved Questions presents a "Question of the Month" on its homepage every month. Set up and formulated by the members of the editorial board, or guest writers, the main purpose of the "Question of the Month" consists in intriguing the reader by presenting topics of ongoing research. "Questions of the Month" published so far cover a wide variety of scientific fields, but share the feature to be of certain interest to several disciplines.
In the following, we present selected "Questions of the Month" from the last six months.

How do odorant sensory cells ensure, they produce only one type of odorant receptor?

Tobias Ruff

Due to technical improvements during the last years, machines outcompete humans in a couple of specialized tasks: Whereas it can take a human person very long to calculate the square root of a (non-square) number, a computer can finish this calculation at high precision within a fraction of a second. However, there are some areas in which machines still cannot compete with nature (yet). One of them is olfaction: Currently, no device is available that could replace police dogs with the ability to detect trace amounts of molecules. Similarly, farmers sometimes even train pigs to search for truffles hidden in the soil. Of course, the ability to detect relevant molecules in low amounts offers an enormous advantage and is thus subject to extensive optimization by evolution.

How exactly olfaction works in higher organisms has not been known for a long time. Nonetheless, it had been intuitively clear that there must be specific receptors interacting with the corresponding odours. This simple assumption has a remarkable consequence: Since mammals can distinguish a high number of odours, there also must be a high number of different receptors encoded in the genome. Indeed, the two scientists Linda Buck and Richard Axel discovered a comparatively large family of genes encoding for odorant receptors.[1] For this discovery, they were awarded the Nobel Prize in Physiology or Medicine in 2004. The activation of these receptors on the cell surface always results in similar intracellular reactions. If a cell had receptors for different odour molecules on its surface, it could therefore not distinguish these odours. In accordance to this consideration, it turned out that each olfactory cell only carries one type of all the different odorant receptors encoded in its genome. Why exactly this is the case is still not known in detail to date. Even more surprisingly, it even turned out that the axons of cells, which carry the same type of odorant receptor on their surface, end on the same set of cells.

Figure 1: L'odorat, Honoré Daumier (circa 1839, public domain – wikimedia).

An odour can of course consist of several kinds of molecules. The activation of different combinations of olfactory sensory neurons further increases the number of differentiable odours. A phenomenon seemingly similar to the exclusive expression of a single odorant receptor by an olfactory sensory neuron is the generation of only one type of antigen receptor by immune cells. They achieve this by a complicated recombination of genes, which is clearly not observed in olfactory neurons.

Investigating how a biological structure develops is often very helpful: In a later work, Linda Buck could show that in contrast to mature olfactory neurons, there are multiple mRNAs for different odorant receptors in immature neurons.[2] Why cells of our body can have entirely different morphologies and properties even though they all carry a copy of the same genome is a fundamental question which keeps many biologists busy. It is the differential expression of the genes in a cell, which causes these differences. This

gives muscle cells the ability to contract and enables neurons to generate action potentials.

However, all olfactory neurons express a very similar pattern of genes except for their odorant receptor. One of the reasons for the transcription of different amounts of RNAs from different genes is the spatial arrangement of the DNA in the nucleus. Had it not been tightly packed into the nucleus, the DNA in each cell would have a total length of 1.8 m and highly condensed sections of DNA are usually not accessible for transcription into RNA. Stavros Lomvardas, a former member of the group of Richard Axel, could show that DNA segments encoding for odorant receptors on different chromosomes get pulled close to each other in a small spatial region in the nucleus. Interactions between the different DNA segments encoding for odorant receptors could contribute to the exclusive transcription of one specific odorant receptor gene.[3,4]

The relevance of the spatial arrangement of the DNA within the nucleus for gene expression is an open question of major interest beyond olfaction. To which degree there is a specific nuclear arrangement of DNA and how this is established after cell division would then be further important for other unsolved questions in biology.

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Gödel's theorem and traffic development

Sergei Sobolev

Intro

Absolute nothingness ($\acute{s}\bar{u}nyat\bar{a}$) is one of the most exciting notions in Buddhism. Essentially, it cannot be interpreted anyhow but can be thought of as Ultimate Reality.[1] In Mediterranean tradition, ancient cosmologists introduced another term that sounds more familiar - The Chaos. It was associated with the infinite ocean and expressed an initial state of cosmos *in potentia*[2]. Not to get numb by the immensity of this semantic unit, we can consider chaos as noise having an infinite spectrum of all conceivable frequencies. And through interaction with external conditions, certain modes manage to become more pronounced as, for example, in the process of stimulated emission build-up in the laser[3] or during the process of natural selection in the theory of evolution.[4]

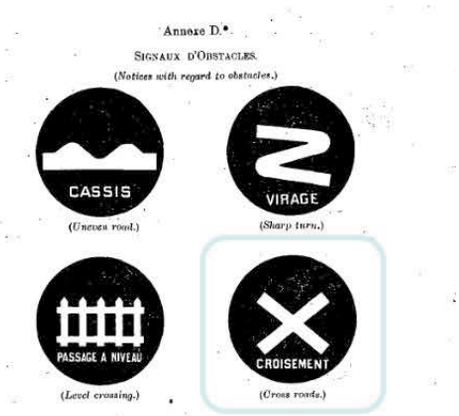

Figure 1: Road signs approved at the Paris convention of road traffic.[6]

Traffic development

In the context of road traffic development, we can define the situation in ancient times as the initial chaotic state. As there were no roads as such, the traffic was chaotic. With the evolution of horse-drawn transport, the road map was developing. However, the roads were still only directions along which one could get from one place to another.

The situation changed when engine cars jolted the slow and stagnant horse traffic. Between the man and the road there was no middle link anymore that could choose a better way within the given direction on its own. Nonetheless, engine-drawn transport had an obvious advantage of higher achievable speed. In turn, the desire to move faster and faster required less scattering at the surface roughness, which inevitably resulted in roads getting smoother, i.e., less chaotic. In the meantime, the assembly line was progressing drastically and both factors lead to a dense cloud of potentially fast cars. But people were still scratching their heads why the average speed of the road traffic was not increasing. After a while, they figured out who is to blame in the residual scattering - the interaction of the drivers themselves with each other. With the absence of any predefined rules, everyone had to slow down and likely change the direction to avoid physical interaction with another participant of the traffic. Thus, the necessity of the traffic regulations was obvious.

The first "Convention with respect to the international circulation of motor vehicles" was signed in Paris in 1909.[5] Among others, it contained the sign depicted in Fig. 1, which indicated the road intersection. And naturally, originating from the ship traffic, the habitual priority-to-the-right rule was established to regulate the right-of-way for two vehicles with intersecting directions. Later a set of traffic regulations was complemented with priority signs and traffic lights.

Gödel's theorems

In 1930 Kurt Gödel presented two theorems reflecting insuperable limitations of formal arithmetics. These theorems had a direct relation to the second problem from Hilbert's list asking for the proof that arithmetics is consistent.[7] The first Gödel's theorem[1] states that within any consistent formal system S, one can come up with expression A that can be neither proved nor disproved[8]. In other words, the axiomatic system S is incomplete. Hao Wang published in his Logical Journey[9] the full text that Gödel had written about his discovery of the incompleteness theorems:

"In the summer of 1930 I began to study the consistency problem of classical analysis. It is mysterious why Hilbert wanted to prove directly the consistency of analysis by finitary methods. I saw two distinguishable problems: to prove the consistency of number theory by finitary number theory and to prove the consistency of analysis by number theory <...> Since the domain of finitary number theory was not well-defined, I began by tackling the second half <...> I represented real numbers by predicates in number theory <...> and found that I had to use the concept of truth (for number theory) to verify the axioms of analysis. By an enumeration of symbols, sentences and proofs within the given system, I quickly discovered that the concept of arithmetic truth cannot be defined in arithmetic. If it were possible to define truth in the system itself, we would have something like the liar paradox, showing the system to be inconsistent <...> Note that this argument can be formalized to show the existence of undecidable propositions without giving any individual instances. (If there were no undecidable propositions, all (and only) true propositions would be provable within the system. But then we would have a contradiction.) <...> In contrast to truth, provability in a given formal system is an explicit combinatorial property of certain sentences of the system, which is formally specifiable by suitable elementary means..."

[1] In Rosser form.

Traffic regulations and Gödel's 1st theorem

We can consider any set of interrelated rules, including traffic regulations, as a formal axiomatic system where each axiom is not subject to prove and serves as a basis for further deriving the formulas and theorems (or behavior in a traffic situation). Clearly, the traffic regulations are consistent because otherwise, the number of car crashes would be much higher. Hence, according to the Gödel's 1st theorem, the system is incomplete. This means that there would always exist a situation, which cannot be resolved regardless of the number of regulations (axioms) contained in the system.

The example of such a situation can be observed on the road intersection regulated by priority-to-the-right rule depicted in Fig. 2. Here four vehicles coming from every direction want to pass this intersection each going straight. There is no way to resolve this situation (to derive the formula) within the traffic regulations system and the drivers in every certain situation are supposed to make the decision: who has the priority.

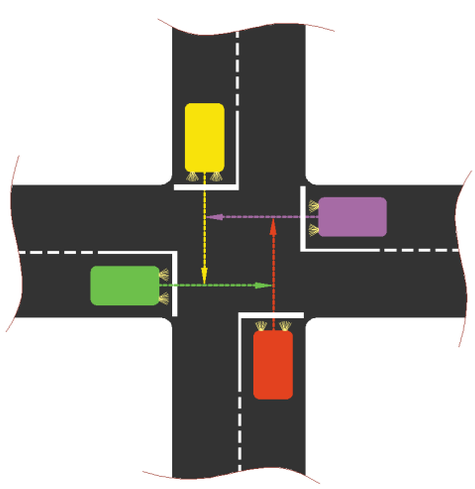

Figure 2: Unresolvable road situation.

We can incrementally enhance our axiomatic system by introducing another rule to resolve such a dead-end situation. A rule that gives priority to go first, say, to a red car. Again, four red cars on the same road crossing end up with the same confusion. As long as we add the rules (axioms) into the system enumerably, which is the case for the traffic regulations, such situations will always appear. Introducing the priority signs, constant or variable in time, like traffic lights, or topological road junctions (see Fig. 3) can only decrease the probability of this situation emerging.

Nowadays, most of the intersections are controlled (or topologically resolved). And let's assume that the preposterous situation with four red cars trying to figure out the right-of-way on the uncontrolled intersection hasn't happened up to the moment in our complex but finite system of road traffic. Hence, the drivers' behavior seems to be fully governed with the traffic regulations. However, there still is a possibility of an unresolvable situation, namely, if one comes up with an expression:"I'm not going to obey the rules". For the axiomatic system of traffic regulations, this expression serves as a "liar paradox" and cannot be resolved. Thus people had to come up with the penalty system for acceptable performance of the traffic regulations. But again, it is impossible to nullify the probability of such a situation emerging.

Figure 3: Topological resolution of left- and right-hand traffic, Pearl River Necklace.[10]

(Instead of a) Conclusion

The aim of this text was not to establish a solid theory in either mathematics or law, and the presented examples may not be in strict compliance with the described statements. However, the author finds entertaining the fact that there are bridges between different islands of knowledge accumulated by mankind over the infinite ocean of the unknown.

Read more:

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How Beneficial is Camel Urine for Human Health?

Tatjana Daenzer

Just the thought of getting in touch with or even ingesting urine repels many people. But medical treatment with urine – also called urotherapy – has been a valuable approach in the traditional medicine of many cultures over the last centuries. Usually, endogenous urine is used but animals are also popular sources. The utilization of urine in conventional medicine is not uncommon too. Urokinase, for example, can be isolated from (human) urine and is an important thrombolytic agent.[1] The drug Premarin®, which is used for hormone treatment, contains estrogens that are extracted from the urine of pregnant mares.[2]

Besides milk, camel (i. e. *camelus dromedarius*) urine plays a special role for desert dwelling people like the Bedouin. Its use was advised by Prophet Mohammed, thus it has found its way into the Islamic prophetic medicine.[3] Apparently, this body liquid cures diseases like tuberculosis, hepatitis, digestion problems, impotence, hemorrhoids, and flatulence, just to name a few. In 2013, one liter of urine from a virgin camel was worth about 15 EUR (ca 20 USD) in Yemen, where it is not only used for universal medical treatment but also as a cosmetic product for skin and hair care.[4]

Figure 1: A Moroccan dromedary camel – a favored livestock of Bedouin people.[5] (public domain – wikimedia commons)

Conventional medicine offers plenty of pharmaceutical cancer treatments which are a blessing and a curse for the patients at the same time. Besides the tedious and exhaustive treatment, patients are confronted with severe side-effects including nausea, fatigue, hair loss, inflammation, and temporary immunodeficiency. The demand for alternatives that are at the same time highly effective, easy to use, mild, and in the best case based on renewable resources is therefore very high.

Camel urine has long been claimed to be an efficient cancer treatment but detailed research on its actual potency and effect on human health is scarce. The soothing effect of pure camel urine on digestive problems can sufficiently be explained through its relatively high content of electrolytes like sodium and zinc as found by Al-Attas, in 2009 – a result that certainly might be achieved just as well by drinking a bouillon.[6] Kohrshid et al. were the first to show an inhibiting effect of lyophilized camel urine on carcinoma cells in animals.[7] In 2011, Alhaider et al. found that treatment of murine hepatoma cells (Hepa 1c1c7, i. e. liver cells) with camel urine inhibited the induction of Cyp 1a1 (a well-known cancer-activator) gene expression by TCDD, a potent Cyp 1a1 inducer and known carcinogen. Among virgin, pregnant, and lactating camels, the virgin's urine was found to be most potent while the urine of pregnant camels showed the least potency.[8] One year later, Khorsihd et al. showed that the potency of camel urine to reduce a specific type of lung cancer cells (A549) is somewhat dependent on the breed (Majaheem urine was found to be more effective than Magateer urine) and the age of the camels. The depletion of the cancer cells ranged between 85–93% of the starting cell number.[9,10] The bioactive subfraction PMF which is believed to be responsible for these effects is obtained from lyophilized camel urine (in literature frequently called PM701).[10] Clinical trials on the oral uptake of PM701 fractions showed no negative effects on human health so far.[11] Apparently, the urine contains a high amount of antibodies of such a small size, that they can be easily absorbed by the patient's digestive system.[12] Other experiments also show antimicrobial effects of camel urine on bacteria and fungi.[13] Aiming at the environmentally friendly substitution of synthetic agents which are usually obtained from complex multistep reactions this approach is most honorable. It is exciting to see that a waste product has the potential to cure severe diseases although much more research must be done on this subject to clearly verify the efficacy. After all, urine is an excretion that contains various less beneficial digestive metabolites, and even toxins that the body wants to get rid of and indisputable evidence for the efficacy and safety of the PM701 fractions are vital.

For those people who are curious enough to try camel urine for whatever reason but are too disgusted by the idea to drink it pure, a solution might be on the way: there are capsules of PM701, or PMF respectively, but they are not yet available on the market.[10] Another alternative might be camel milk which sounds much more enjoyable and is supposed to be a medicine just as magical as camel urine. It is said to "reduce blood sugar [...] solve the problems of autism in children, enhance the immunity of the body..." and many more.[14] Alas, some bad news comes from the World Health Organization (WHO) concerning the use of camel milk and urine: shortly after the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in Saudi Arabia in the year 2012 dromedary camels were found to be zoonotic transmitters, meaning that the virus is rapidly transferred from animals to humans.[15] As a consequence

the WHO advises to avoid contact with camels or consuming raw camel milk and urine.[16] This surely dampens the enthusiasm to utilize camel urine and we might have to wait a few years more for some groundbreaking results in cancer research.

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Why do your pipes sometimes bang when you turn off your faucet?

Kai Litzius

You might have encountered the phenomenon: You have a faucet running, for instance, while filling your bathtub, and quite a bit of water is flowing out. Then you want to stop the flow and quickly turn the valve to block the water. Suddenly, in the very moment you close the valve, you hear a banging sound in the walls around you. Sometimes it is rather quiet, sometimes it can be scarily loud. But what is actually causing the sounds and is it something you should worry about?

It turns out that the answer to this question is one of the most relevant design considerations for civil engineering.[1,2] It all roots in a fundamental property of liquids: not being compressible. You may have noticed that a balloon filled with air can be compressed quite a bit while one filled with water only changes shape and cannot be made smaller. This very principle is the core of hydraulics, i.e. using the volume of a liquid like water or oil to transfer force in a system.

Maybe you are wondering now how this affects your pipes, considering that the volume of the pipe always stays the same. Nobody (hopefully) compresses the pipes in your walls. There is, however, also another important aspect to a liquid: its momentum. Once a liquid starts to move through a pipe it builds momentum just like a car or a train build momentum when they move (see Fig. 1). As long as the flow can continue undisturbed no ill effects occur and similarly, nothing happens if the flow is slowly brought to a halt by gradually closing the valve. To stay in our analogy, this would correspond to a train of cars slowing down when a road gradually narrows from two lanes to one and eventually to a road blockage.

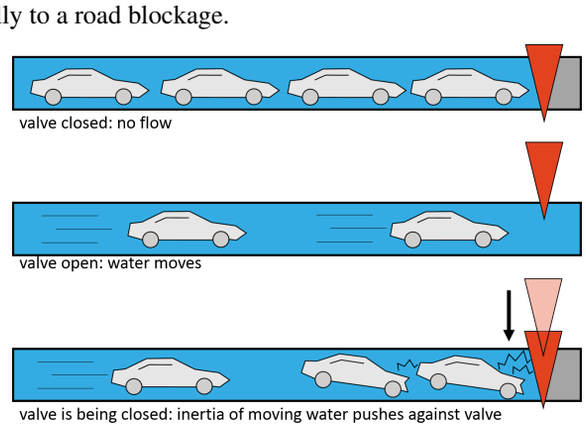

Figure 1: Analogy of moving water and a train of cars. When the water is still, no momentum is stored in the system. Once the water moves, a significant amount of inertia can be present in the flow and if that flow is suddenly restricted by something (like a valve), the entire inertia must be transferred to the environment. That is the walls of the pipe and the valve itself. ©JUnQ.

The interesting effects happen when we force the flow of liquid to stop suddenly with a valve, essentially causing an accident on our road that causes all the cars to slam into the blockage. In this case, a rather large amount of inertia must be dissipated into the valve and the walls of the pipe causing a large pressure spike. If the pipe can move like a free garden hose (e.g. old pipes that are not properly fixed) this can lead to a sudden jerk and might loosen connections. The story is not so easy, though, for pipes that are fixed in your walls or buried beneath streets: those usually cannot move. As a result, the full force of the pressure acts on the valve and the walls of the pipe – causing the banging sound in your bathroom. The effect is officially called 'water hammer'.[3]

But before you start wondering now if your pipes will one day burst and start flooding your apartment: civil engineering has developed a series of safety measured to prevent this from happening in our daily life. To understand how, it is important to know that the pressure spike caused by the sudden restriction in water flow is directly related to the flow rate. In our car analogy this would correspond to the relation between the number of lanes on the road and the number of cars that have to pass through a road segment at any given time. Together this dictates the speed the cars are traveling with and their cumulative inertia. In simple words: fast-moving cars on a narrow street do have a much harder time to slow down than a larger number of slower cars. Therefore, many supply pipes have large diameters, causing the water to flow slowly and thus avoiding the pressure spikes if the flow is restricted by one of the recipients. Additionally, air or spring-loaded pressure relief valves can engage to dissipate a dangerous spike without causing damage and water suppliers usually have build-in safety measures to make sure pumps are not starting up too quickly.

All in all, you usually do not have to worry about a slight banging sound caused by quickly closing a faucet, even though you should avoid it if possible. However, if it is loud or suddenly starts to appear you should be careful to reduce the wear and tear of your pipes or directly ask a pumper. A neat little starting point is Ref. [1]. Anyway, next time you use your sink or shower, think maybe of all the civil engineering that is necessary to let you shower or take a bath anytime at will.

Disclaimer: This article is meant to give an introduction into the physics behind the water hammer. In doubt always ask a specialist if your piping needs to be repaired.

Read more:

[1] https://home.howstuffworks.com/home-improvement/plumbing/how-to-fix-pipes5.htm
[2] https://www.youtube.com/watch?v=xoLmVFAFjn4
[3] A similar effect occurs with steam, the so-called 'steam hammer', which is an exceptionally dangerous phenomenon that can lead to steam pipes exploding once too much steam condenses and the condensate gets accelerated through the pipe. See also here for a great explanation: https://www.youtube.com/watch?v=JyvoN1hIqRo

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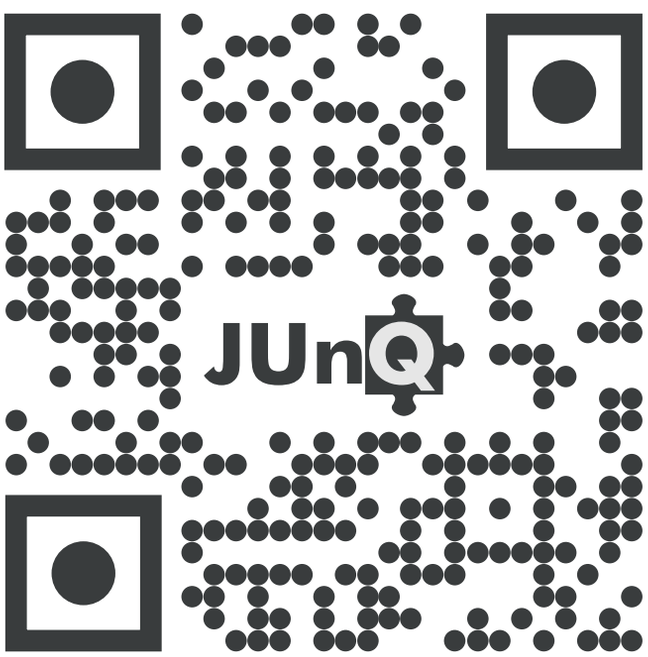

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