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Serendipity in Astrophysics - interview with Dr. Patrick Kelly

“Well, That’s Strange…” or the History of Many Happy Accidents

Delicious Craft - interview with chef Artem Chudnenko

Serendipity - a Liaison of Luck and Science

“You didn’t expect that?!” - Survey

SERENDIPITY

Table of Contents

Preface

Editorial Note

"The most exciting phrase to hear in science, the one that heralds new discoveries, is not "Eureka!" but "That's funny…"

Isaac Asimov

Dear Reader,

Sometimes we struggle to find the answers we are looking for. In the end, we do not find them but discover something else. It might seem like a background noise in the data at first but while taking a closer look it turns out to be a real thing. That is how some discoveries are made. A forgotten sample on a window sill, a result that defies the calculated estimations, an identification of a critical condition during a routine medical examination. These are all examples of serendipity-driven discoveries. In the history of humanity, serendipity is a vital phenomenon that helped us evolve and still finds its way into the modern scientific culture. In this issue, we will take a closer look at serendipity, how it has helped to make important discoveries and the role it has played in your endeavors. Moreover, we will discuss the serendipitous outcome of stargazing with Dr. Patrick Kelly and see what other role one's guts can play in the kitchen in an interview with chef Chudnenko. The main message of this issue is to stay alert and mind the details. Who knows what you might find?

— Kevin Machel

Opinions

Serendipity - A Liaison of Luck and Science

Kevin Machel

Serendipity is the product of an interplay between chance and wisdom. It has accompanied us since the dawn of mankind. At first, discoveries were made by mere chance as e.g. the discovery of cooking food with fire. Over the millennia, humans started searching more systematically for answers and solutions. In the last centuries, this systematic search developed into what we know as the scientific method. With that development, the ratio between chance and wisdom changed. Now, in the 21st century, serendipity is being re-discovered. It becomes a new tool in accelerating scientific progress, as young scientists use serendipity as a method to gather answers they never looked for.

The term Serendipity was coined by Horace Walpole in 1754 in the correspondence with his friend Horace Mann about an old Indian fairy tale. He wrote to his friend about the tale of "The Three Princes of Serendip" where the princes discover evidence for a camel theft by mere chance during a stroll. Hence, Walpole used the name of their Kingdom "Serendip", which is the old name for the region of Ceylon, to describe finding something you were not looking for.[1]

Figure 1: Three Cinghalese Chiefs Waiting for the Prince of Wales at Kandy, Ceylon. The aristocrats may help to picture the local attire of "The Three Princes of Serendip".[2]

In the age of enlightenment, it was common for wealthier people to conduct experiments, solve math riddles, or tinker in home labs. Many people in different countries were working simultaneously on similar questions discovering little pieces of big puzzles. On a large scale, this was a systematic approach to making discoveries and progress. On a small scale it were people pursuing their curiosity through conducting various experiments. All these experiments served to piece together the foundations of modern science like e.g. the periodic table of elements. This accounts for engineering as well, take for example the development of the microwave that started with a molten chocolate bar oven or steam- and petrol engines. All these crucial discoveries were made through luck and trial and error. And an environment of trial and error serendipity serves as a key to a treasure chest that no one expected to find.

One other well known example is the discovery of X-rays by Wilhelm Conrad Röntgen. Inspired by earlier experiments, the German physicist was studying the phenomenon accompanying the passage of an electric current through a gas of extremely low pressure in evacuated cathode tubes. These streams of electrons were called cathode rays and, at that time, they were well known, although their nature was still debated. Knocked out from the cathode material the electrons travel in straight lines through the evacuated tube and a high voltage accelerates these light particles to high velocities. Normally they are invisible, but their presence can be detected due to their interaction with the glass wall of the tube, known as fluorescence. When cathode rays strike the glass, the orbital electrons of the glass atoms are excited onto higher energy levels. Then, as the electrons return to their ground states they release energy in the form of light, causing the glass to fluoresce, typically emitting a dim greenish or blueish glow. Later, it was common to paint the inside of the walls with fluorescent chemicals to enhance the glow.

Thus, Röntgen's idea was to study the resulting luminous effect by experimenting with different fluorescent materials. In essence, Röntgen just wanted to investigate the details of a known phenomena. But his work on cathode rays led him to the discovery of a new and different kind of rays. Preparing for the experiment, Röntgen covered the tube completely with black paper and switched off the lights. He was satisfied that the room was completely dark as he applied the high voltage between the electrodes. That was until he noticed that further back in the room there was a green glowing smoke.

Completely baffled he lit a match and walked towards the green glowing smoke. As he approached the source he realized that a paper plate covered with fluorescent chemical that he planned to use further on in his experiment was emitting the green glow. He could not explain this since the tube was completely covered to exclude all light from fluorescing glass walls, and it was known from the previous experiments that the cathode rays could not escape the tube. During subsequent experiments he found that the fluorescent plate would glow even when it was as far as two meters away from the tube. In addition, he discovered that different materials of different thickness placed in the path of the rays showed various transparency to them when recorded on a photographic plate.

Figure 2: The first anatomical X-ray photo by Wilhelm Röntgen (1845–1923) of the left hand of his wife Anna Bertha Ludwig.[4]

At last, he even asked his wife to put her hand into the path and captured the first ever x-ray image that showed a dark seemingly distorted shadow of her hand. Immediately Röntgen realized that her hand was not distorted as such but that it resembled the skeletal structure of the hand. He concluded that primarily the skeletal structure was able to dim the responsible rays. The nature of this new kind of rays was so strange to him that he named them "X-Rays". Within one year after the discovery by Röntgen, lots of books and hundreds of articles were produced and the newly discovered rays were utilized in medicine. Never before was a newly discovered phenomenon implemented so fast. And all of that because Röntgen noticed something unexpected. He could have easily missed the dim green glow as maybe others had before him. But chance was on his side that day. In addition, he realized that he saw something real and new that needed to be characterized.[3]

Since the beginning of the 20th century, a lot has changed in the way we perform science. Nowadays research is executed with much more focus on careful strategic planning of the projects. Still, chance plays a major role in facilitating developments and can sometimes be the spark that incites a revolution in a field. One example that took place not so long ago is very well known for its impact on biology, medicine, and related fields. The discovery in question is of course CRISPR (clustered regularly interspaced short palindromic repeats). This discovery was not made by one group by accident but by a multitude of unrelated researchers. As a fresh Ph.D. student, Francisco Mojica was investigating the influence of salt concentration on the regulation of genes in *Haloferax mediterranei* bacteria. Incidentally, Mojica noticed that he found certain DNA fragments with similar size and symmetry time and time again. He dubbed them short regularly spaced repeats (SRSRs). Soon, he found similar SRSRs in more than twenty different bacteria, some of them completely unrelated to each other. He quickly realized that he had stumbled across something of fundamental importance. In the following years, Mojica tried to discover genetic patterns matching those of CRISPR to identify their interaction partners. In the beginning, he did not find anything, but with new DNA sequencing technologies emerging, the databases on genetic information grew rapidly. In 2003, Mojica succeeded in finding matches but not in the bacteria itself, but bacteriophages. From these matches, he concluded that CRISPR seemed to play a role in the immune response against the corresponding bacteriophages. We included a chart below to visualize this mechanism of action.

Roughly at the same time, Gilles Vernaud from the French Ministry of Defense found that "CRISPRs may represent a memory of past genetic aggressions" while researching plague bacteria to develop an identification system for bioweapons.[5] Although these projects lay the foundation for understanding the CRISPR system and its function, the articles concerning these findings were rejected multiple times because of the lack of novelty for the most part. The last puzzle piece that sent the research topic flying was that Phillipe Horvath was investigating phage-resistant bacteria for Lacto fermentation of Sauerkraut. He discovered the research around the CRISPR system and tried to actively make a strain of bacteria resistant against common phages by exploiting the system and inserting the genetic pattern of the phages into the CRISPR loci. After this experiment was successful it was evident which power CRISPR might hold. It was now possible to create and cultivate CRISPR systems that can edit DNA selectively. None of the three researchers in question ever investigated methods of genetic editing. None of them ever had in mind what possibilities CRISPR would enable for research, they just found some odd results along their path and decided to take the risk to investigate them instead.[5]

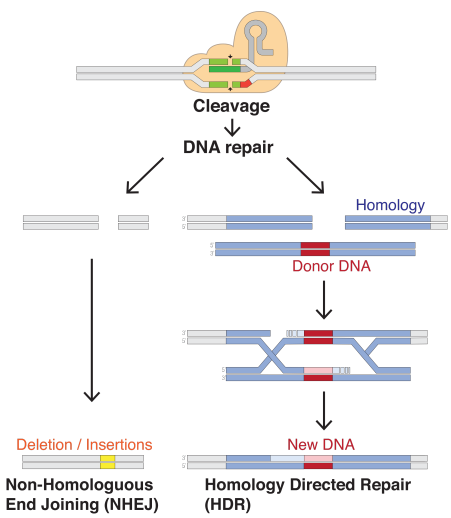

Figure 3: General mechanism of action of the CRISPR-CAS9 system. The "Immunity" is gained by cutting out the genetic code inserted into the bacterial genome by the phages. Simultaneously genetic fragments of the phages are stored in the CRISPR-Loci for future recognition and response. Credit: Marius Walter, Biologist with an interest in genetics, epigenetics and virology. Copyrighted work available under Creative Commons Attribution only licence CC BY 4.0.

In the wake of harnessing AI and data mining software to dig through enormous amounts of scientific data lays the great potential for increased serendipitous discoveries as in the case of Mojica. Since chance plays at least a lowkey role, in order for someone somewhere to notice the one odd data set, an increase in data processed might lead to more serendipity events. In the case of Mojica it worked out because he knew what he was looking for. However, the use of common data mining software might prohibit serendipitous findings. Most of the commonly used programs require specific training or accurate definition of what to look for. Therefore, the need for "serendipity-sensitive" programs is evident. A question that remains open: are we able to teach programs to recognize the unknown pattern in the data to sort it out for further investigation? In recent years, there have already been successful attempts to train systems to be on the lookout for serendipitous events or at least promote serendipity. The next step in this regard is to broaden the application of these systems to crunch the experimentally obtained numbers for researchers to get serendipity back into the data evaluation of the 21st century.[6]

Since serendipity seems to be such a crucial factor for the promotion of science, it is of no surprise that a whole new field of serendipity science formed in recent years. One famous example is Pek Van Adel, who strongly promotes the principle of serendipity. Throughout his career, his focus of research included not only medical forensic studies but increasingly the phenomenon of serendipity. In 1999 he and colleagues playfully investigated the question of how it would look if two adults were having sex in an MRI scanner. That question was answered and revealed quite astonishing new insights into the mechanism of action that were not expected generally by gynaecologists and dismissed in previous theories. Furthermore, this investigation won him an Ig-Nobel prize in 2000 to credit his curiosity. He and others were able to describe certain patterns of serendipity in order to increase its probability of occurring. One of these patterns, the "analytical serendipity" can be described as the capability, arising from past experience, to discern a new discovery and understand its significance, as in the example of X-rays. In addition, the "temporal serendipity" explains the synchronistic occurrence of events to play together, as in the example of CRISPR. The third pattern, the "serendipity relations" can be distinguished by its social nature. Every time we meet someone unexpectedly, they coincidentally become a future source of inspiration and sometimes meeting just the right people can lead to a discovery. In reality, though, there is not only one serendipity event but many small events following these patterns that enable us to make the discovery. Knowing that these patterns exist enables us to promote serendipity even in our modern scientific culture. Therefore, serendipitiologists like Pek Van Andel describe virtues that a researcher must embrace in order to cultivate serendipity. With the work of Van Adel and others, centuries of knowledge are condensed and enable today's scientists to utilize knowledge of the past for the discoveries of tomorrow.[1,7,8]

From past to current-day experiences we have seen that serendipity is difficult to grasp let alone to control. But there are quite simple things we can do to promote it. From the patterns and virtues defined by Pek Van Andel to more intuitive subtle actions, we can adopt routines to be prepared for the moment serendipity strikes. Sometimes we should take a step back, be brave and investigate that weird signal or that small peculiar detail. We should take the time to wholly understand our results and experiments and not just run from the lab to the desk to start piecing the paper together right away. Ultimately, we do not have infinite time and we have to come to a finish line on a project. But these couple of extra minutes as in the case of X-rays or CRISPR might be worth the shot. Even more important is a network, as evidenced by the case of CRISPR. Only if we can access information easily and at the right time, can ideas form and projects become connected. Finally, it is a question of scope. One can only stay alert so much in one's research. But if we want to promote serendipity we also have to develop systems or programs that identify interesting previously unknown patterns in the information that is found by all researchers. With new tools in development on this matter, the future of serendipity seems very bright. Therefore, stay alert and who knows what you might find.

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“Well, That’s Strange...” or the History of Many Happy Accidents

Tatjana Daenzer

Whenever scientists begin their experiments, a lot of time and brainpower has been invested in the preparation beforehand to ensure that everything goes right. Not only do they wish for positive results, meaning (in chemistry) high purity and high yield, but also a safe performance of their syntheses without unexpected events. Rigorous cleanliness and thorough research ensure success. But way too often the reaction vessels are not clean, or the necessary safety precautions are not met. Those who were so lucky not to set the lab on fire were sometimes even luckier to obtain something better than they were looking for. Daring curiosity is a human characteristic. Provokingly spoken, far before people conducted research as we know it today, chemistry – or alchemy – meant fooling around with whatever material was within reach, often without any factual knowledge to begin with. In fact, most of the basic materials on which we build our lives were the result of a little happy accident or just plain trial-and-error.

Glass occurs naturally in the form of some types of quartz, obsidian (an igneous rock that it is formed during volcanic eruptions) or tektites that were formed by meteoric impacts on the earth’s surface millions of years ago. It is a non-crystalline (amorphous) material, meaning that its molecular structure is not entirely ordered, resulting in transparency. Industrially it is obtained by smelting quartz sand, carbonates, and other trace minerals at temperatures around 1400 °C. It is not recorded who produced the first artificial glass. But archaeological findings suggest that it was already produced around the Eastern Mediterranean region of Western Asia between Egypt and Mesopotamia about 6000 years ago. According to a tale, “nitrum” (Latin for sodium hydrogen carbonate or natron) merchants were resting on a beach at the Syrian coast. Some nitrum lumps fell into the sand below their campfire, fusing to liquid glass.[1] The temperature of a simple campfire, however, should not be able to melt sodium and sand (which is mostly consisting of silicates or quartz) this easily. Other sources report that the early glass was a byproduct of metal or pottery production.[2] The heat that is needed to melt down ores is more sufficient to melt down silicates. Together with some impurities like salts and other minerals, that could have stuck to the ores, some grains of sand might have merged into some tiny beads of glass. The raw material was not that rare or expensive, but a lot of effort must have been put into finding out the right mixing ratio to gain clear, or even colorful glass. Thus, glass was a highly valued material for jewellery, comparable to actual gemstones. Nevertheless, both stories indicate that the discovery of glass production was a coincidence rather than a knowledge-based invention.

We don’t have to go too far back in history to find another phenomenon that was revealed by mistake but made a world-changing impact that we still can feel today: the discovery of vulcanization in 1839 by Charles Goodyear.

Rubber is a natural material that is harvested from plants. But in its raw form (also called latex), it has no desirable properties. On cold days it is brittle, on warm days it is a sticky liquid, and it stinks. There was, however, a commercial interest in a material that was elastic as well as weather- and waterproof, so Goodyear conducted experiments with latex and other substances to make the former more durable. Only by accident, he dropped a mixture containing latex and sulfur on a hot surface. Curiously, the mixture did not burn or evaporate, but formed a flexible goo that was stable at a convenient temperature range and could still be brought into a desired form. What the sulfur caused was “simply” a connection of the long chains of which the rubber is made of on the molecular level to form a cross-linked, flexible network. The method has been refined and still today new high-tech rubbers are developed.[3,4]

The serendipitous story of rubber goes even further. In search for a cheap substitute of rubber during WWII, Rob McGregor, Leathen Warrick and James Wright independently experimented with polysiloxane (silicon oil) and boric acid. The result was entirely nothing like the rubber that we use for tires and boots. But it was fun! They obtained an expandable soft mass that bounced when thrown on the hard ground but started to run after being left on a surface for some minutes. The material did not have any properties that were of industrial or military interest. But together with color, glitter, and even magnetic particles it later made a nice toy called “Silly Putty”.[5,6]

Figure 1: Moldavite, a tektite found in the Czech Republic (left), a glass flask of roman origin from 1.-3. AC (middle), and a flask commonly used in the lab made from a highly durable borosilicate glass (right).[7-9]

The decades that were overshadowed by the world wars were also inspired by a search for all sorts of cheap substitute materials. The first gas absorption refrigerators used liquefying gases like ammonia or sulfur dioxide as refrigerants. The leakage of these substances was certainly no fun. It did not take too long to discover that non-toxic, non-flammable and odorless refrigerants could be synthesized: the chlorofluorocarbons (CFCs). In 1938, occupied with the development of new CFCs, the chemist Roy J. Plunkett experimented with tetrafluoroethylene gas. When his gas cylinder suddenly clogged, he discovered, that the gas inside had been consumed to form a non-adherent, inert, and colorless solid: polytetrafluorethylene (PTFE). Apparently, the pressure together with the catalyzing effect of the metal of the cylinder wall led to a rapid polymerization of the gas. Although it was not suitable as a refrigerant, PTFE was quickly patented for its various beneficial properties, most of all its resistance to heat, the extremely low coefficient of friction (that means it is so slippery, that even geckos can't hold a grip on a PTFE surface), and chemical stability.

PTFE went down in history, known under the trade name "Teflon" and still amazes cooks, plant manufacturers, and electricians all over the world.[10-12]

Again, it was a huge coincidence and a little bit of untidiness that led to another lucky (re)discovery, this time of a pharmaceutical treasure. Around the 1860s and 1870s, some research was conducted on the behavior of bacteria and fungi. Inspired by an episode with a patient who successfully treated a nasty ulcer with a broth of figs and milk, the German surgeon Theodor Billroth decided to experiment with bizarre broths as culture media for molds or fungi. He observed that a certain type of mold, the *penicillium*, prevented certain bacterial cultures (*cocci*) to grow in a medium. Around the same time, John Tyndall and Sir John Scott Burdon-Sanderson, both British amateur microbiologists, came to the same conclusion with their research. But it was not yet the time to deduce a correlation between infections, bacteria, and penicillin. The knowledge went by the board for decades because working with mingled microscopic cultures was not considered to be "true" science.[14-16]

Figure 2: A lump of Silly Putty slowly dripping through a hole in a screen.[13]

The medical breakthrough had to wait for another roughly 50 years when Alexander Fleming, a Scottish physician, left some *staphylococcus aureus* cultures in a medium on his bench exposed to the air and went on holidays. When he came back, he noticed that one of his medium plates was “infected” with *Penicillium glaucum* which inhibited the bacteria that were too close to it to grow. It took some more years and some more brainpower to transform penicillin, as it was then called, to an ingestible drug for *in vivo* applications that was also producible in large quantities. But then, the triumphal march against otherwise painful or deadly infections like meningitis and syphilis was unstoppable.[15,18-20]

By the way, Fleming also discovered lysozyme (an antibacterial enzyme that plays an important part in the immune system) - by chance. For the discovery of penicillin, he and his co-workers received the Nobel Prize in Medicine in 1945.[21]

Figure 3: A short section of polytetrafluorethylene and an old advertisement for a teflon-coated pan from the 1960s.[17]

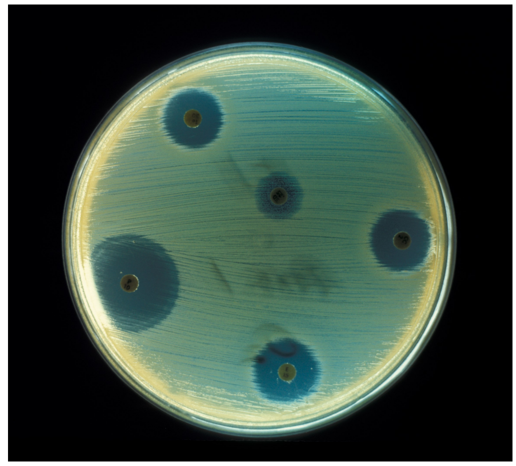

Figure 4: Substrate covered with Staphylococcus aureus. Antibiotics are dispersing from the discs of mold, preventing the bacteria from growing around them.[22]

The color blue has fascinated mankind across all eras. For about 40% of all people, it seems to be the favorite color.[23,24] Synthetic blue pigments based on minerals have already been known by ancient cultures like the Egyptians and the Chinese.[25] Today, we still use Prussian blue (Iron(III) hexacyanoferrate(II)), cobalt blue ($CoAl_2O_4$), ultramarine ($Na_{8-10}Al_6Si_6O_{24}S_{2-4}$) and indigo. Prussian blue was discovered in the early 18th century, when Johann Jacob Diesbach, a swiss pigment producer, attempted to make “Florentiner Lack”, a red varnish. The process involved the use of iron(II) sulfate. When potash was applied to clean up the product, the color of the batch unexpectedly turned deep blue. Diesbach asked his supplier Johann Konrad Dippel, and apparently, he accidentally delivered potash that was contaminated with animal fat and hexacyanoferrate, which did the actual trick. A little later, Johann Leonhard Frisch refined the synthesis and made it ready for the markets. Since he was from Berlin in the former state of Prussia, he named it “Prussian blue”.[26]

The student William Henry Perkin had similar luck in 1856 when he initially was looking for a way to synthesize quinine, a possible treatment for malaria. He attempted to oxidize aniline but the reagents which he used were contaminated with toluidine and the reaction resulted in a dark purple instead of a colorless precipitate. Mauveine was born and it was an excellent substitute for the expensive natural red dyes. Perkin patented his aniline-based dye and founded an own company at the age of only 18. In the end, this was the origin of some of today’s largest chemical companies, above all the “Badische Anilin- & Soda Fabrik”, BASF for short.[27-29]

The run on new brilliant synthetic pigments is not yet over and still relies on "happy accidents". Andrew Smith was conducting his experiments in the lab of Prof. Mas Subramanian at the Ohio State University on the magnetic behavior of different manganese oxides and their solid-state mixtures. For their preparation high temperatures above 1000°C are needed. When Andrew Smith pulled his baked samples out of the furnace, one of them was vividly blue. Upon further investigation the substance proved not only to be beautiful, but also chemically stable and non-toxic. The main components are yttrium, indium, and manganese (chemical formula: $YIn_{1-x}Mn_xO_3$) and depending on their ratio, the darkness of the color can vary significantly. The pigment is already commercialized, and the company "Crayon" has given it a name that is more suitable for marketing: "Bluetiful".[30-32]

This article can only give a short glimpse at the many happy coincidences that led to groundbreaking inventions. It is clearly an achievement of humankind not to throw unexpected and even undesired outcomes in the trash but to see some greater use and value in them. Hopefully, there will be many more of those accidents in science to further our relation to nature. Just imagine all the serendipities that still await us. Nevertheless, stay safe and curious!

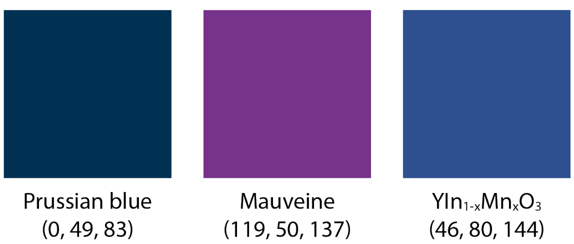

Figure 5: The different shades of synthetic pigments and their respective rgb code in the brackets below.

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Serendipity in Astrophysics

Dr. Patrick Kelly[1] is an assistant astronomy professor in Minnesota Institute for Astrophysics. During his postdoctoral time at Berkeley he made his first serendipitous discovery of the first gravitationally lensed distant supernova, using the Hubble Space Telescope. This, in turn, led to further discoveries with tremendous scientific impact in the field. This interview discusses a personal story of serendipity in astrophysics which illustrates that luck comes to those who are prepared to welcome it.

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JUnQ: Let's start from the beginning. Can you tell us in simple words what the discovery from your Science paper[1] in 2015 was about?

Patrick Kelly: Actually, the discovery was in 2014 and the paper came out in 2015. When I was a graduate student, I studied weak gravitational lensing by galaxy clusters. Weak gravitational lensing refers to the case where you distort the images of background galaxies, but not multiply image them. But you still can measure the masses of galaxy clusters, and then matter distribution in a unique way, which is a very useful tool to study the distribution and total amount of dark matter in galaxy clusters. As you know, we cannot detect dark matter directly, but we can detect its gravitational effect. Before that, I studied supernovae as an undergraduate student at Harvard working with Bob Kirshner. At Stanford, a postdoctoral scholar I was working with suggested that I could help out with a new project with the Hubble Space Telescope that Prof. Tommaso Treu was starting. The focus of the project, called the Grism Lens-Amplified Survey from Space (GLASS), was to take spectra of galaxies that were gravitationally lensed using the instrument on Hubble. I was the transient supernovae person on the team as I was looking for supernovae. So, we found a couple and, then, we happened to find this one which was very special. We could immediately see that there were three bright images (Fig. 1).

Of course, for supernovae everything to some extent is serendipitous because you cannot in general predict when stars will explode. Although, in the case of this supernova we were actually able to predict for the first time that a supernova would appear in the sky, when we predicted the reappearance. So, it is a very interesting twist on your serendipity. Because with this very serendipitous case we were able to make an actual prediction.[2]

After that we spent a lot of time in understanding what was happening. In fact, related to this discovery was another serendipitous discovery in the same field which I also made. We were taking images of this multiply imaged supernova over a long period of time. It was something that hadn't really been done before with the Hubble space telescope looking at the same cluster lens for a year every couple of weeks. So, we actually found a new phenomenon – the microlensing of an individual star at a cosmological distance, which in this case was more than half-way across the universe. And that was another serendipitous discovery.

JUnQ: What was the original plan for that project?

Patrick Kelly: The data were taken by the Hubble space telescope as a part of the GLASS program. Every image was taken once a month or something like that, and each field we'd returned to once. So, we had multiple images of them, and they had already been imaged by other programs of Hubble. And the goal was… Well, we all knew that it would be wonderful to find one of these supernovae, but the probability was low. So, in that sense we knew we were looking for something like this, but we didn't have any hope we would actually find it. Whereas actually the discovery of the star - no one was really looking for that. That was even, I would say, more serendipitous. So, I guess we knew that there was a possibility this could happen. There is another crazy thing about this supernova. If you have a gravitational lens, you can get multiple images of the source if it is aligned in a certain way. But here we get multiply imaged both by the galaxy cluster and by a galaxy in the galaxy cluster. So that was even less likely and this is probably why it is so spectacular. The image looks amazing.

JUnQ: How did it feel, the moment you saw the image? Was it difficult to realize, persuade yourself that it was something real?

Patrick Kelly: In this case it was immediately clear that it was very exciting. There were multiple images and I think I emailed everybody right away. Also, on the team, they were all very excited. And then we didn't get much sleep for the next couple of weeks. The data all become public immediately for this particular program. And you try to analyse them quickly because you know that other people may have seen them too, so you want to publish them quickly. But it was a lot of fun.

JUnQ: What kind of impact did this discovery have on your career and the field in general?

Patrick Kelly: The scientific impact hasn't been realized yet. I was working on a couple of papers to measure the expansion rate of the Universe using the supernova. And hopefully those will be very exciting for people. There are also some interesting things that we figured out with a very careful analysis. But they are not published yet.
For career - there were a couple of us. For sure it helped me to find a permanent job, I have no doubt. So, it was a great thing for me. And, especially for the second author on that paper, Steven Rodney. He is also an assistant professor now. He made a huge contribution as well so, I am sure, it was very helpful for him to have found it.
It is just kind of fun for the field. Because a lot of people got very excited about it, making the predictions. There is a paper by Tomasso Treu who collected the predictions from the community.[3] There are different ways to model the dark matter distribution. So, this discovery gives us a unique opportunity to test the quality of the current models by conducting a textbook-like falsifiable experiment. That is the Karl Popper's idea[4] of falsifiable prediction, which you can do in science especially in astronomy very often. So, we are still working through the implications and we are trying to be very careful.

JUnQ: Did you have more of these lucky discoveries?

Patrick Kelly: Certainly, the discovery of the star. I never thought we could see individual stars across the Universe. It seemed totally crazy. So that was lucky.
And then for other papers I feel like we were lucky to make some kind of discoveries, but it was not like we found an individual object. Probably a lot of the things are lucky, because you look at the right time and you have the right skills.

JUnQ: Making successful discoveries in astronomy is not comparable to buying a lottery ticket, right? What is generally needed for luck to strike someone? How can one be prepared?

Patrick Kelly: Part of being prepared is to have a good team of collaborators. Because everyone has different expertise. For us, there were people who were supernovae experts, people who were modellers of the dark matter, and gravitational lensing experts and galaxy experts. Pulling all those people is important. Because then you can rapidly interpret what is going on. So, I think it is a really important piece.

JUnQ: There are hundreds of research papers having "serendipitous" in the title. But yours does not, why is that?

Patrick Kelly: I think it is because in part one can never predict (with the exception of our own prediction) when a supernova or a star will die or explode. That's how transient astronomy works - you never know when something happens. So, you try to put yourself in a position where you could find something exciting. And that was what we were trying to do. It wasn't even the main driver of the science program. We were just lucky in that it happened while we were observing, but it was not completely unexpected I would say.

JUnQ: Astronomy seems to be the field of science where chance discoveries certainly play an important role. How do you think the advances in machine learning and artificial intelligence will impact the chances of serendipitous discoveries?

Patrick Kelly: We are looking at various things that are exciting and intrinsically rare and that haven't been seen before. You certainly are going to find more of those if you do more searches and collect more data.

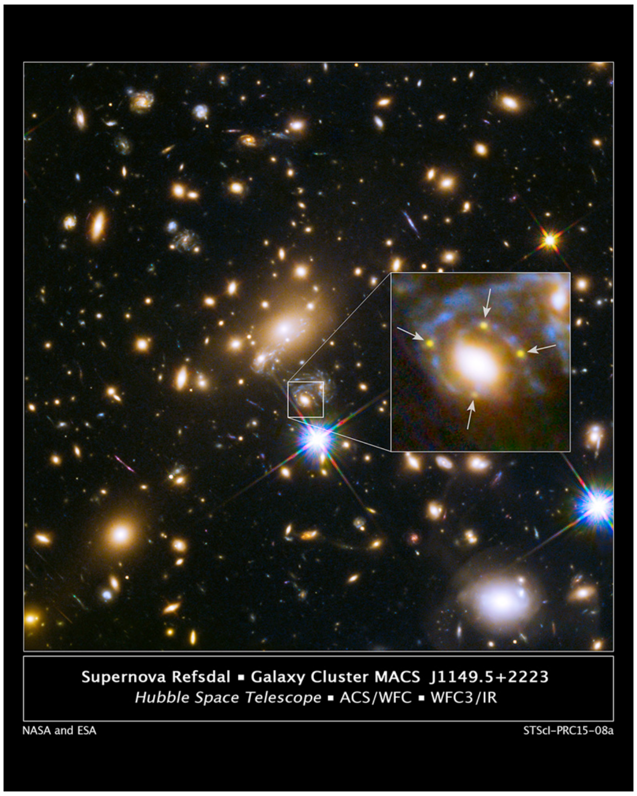

Figure 1. The image shows a part of the deep field observation of the galaxy cluster from the Hubble Space Telescope. The many red galaxies are members of the massive MACS J1149.6+2223 cluster, which creates distorted and highly magnified images of the galaxies behind it. A large cluster galaxy (center of the box) has split the light from an exploding supernova in a magnified background galaxy into four yellow images (arrows). Image credit: NASA, ESA, and S. Rodney (JHU) and the FrontierSN team; T. Treu (UCLA), P. Kelly (UC Berkeley) and the GLASS team; J. Lotz (STScI) and the Frontier Fields Team; M. Postman (STScI) and the CLASH team; and Z. Levay (STScI).

So, I think we will start finding more crazy things for sure. And even if each of them has low probability, if we look enough, hopefully we will find more of them. In astronomy, there is a movement towards wider and wider field telescopes. One of the new NASA missions is called the Roman space telescope, previously called W1. It has a field of view of a hundred times Hubble's. So, it should be able to discover a hundred times more transients.
I was searching the data from Hubble by eye. When we scale it up like this, we'll certainly need some machine learning and certainly software to help. But I think it is a challenge for sure. We will see, we should find interesting things.

JUnQ: Do you have some advice on how to be lucky?

Patrick Kelly: I guess you never know what could be around the corner and it is a reason to be optimistic. But maybe I am just lucky in this case. It seems like luck is an important part of science for experimentalists. So, you just try your best.

JUnQ: Thank you very much for the interview!

— Mariia Filianina

Read more:

[1] P. L. Kelly et al. *Science*, **2015**, *47*, 1123–1126. DOI: 10.1126/science.aaa3350.

[2] https://en.wikipedia.org/wiki/SN_Refsdal.

[3] T. Treu et al. *The Astrophysical Journal*, **2016**, *817*, 60. DOI: 10.3847/0004-637X/817/1/60.

[4] K. R. Popper, *The logic of scientific discovery*. (Translated from German original: Logik der Forschung. Zur Erkenntnistheorie der Modernen Naturwissenschaft). **2002**. London: Routledge.

Delicious Craft

Artem Chudnenko[1], the chef of the restaurant “Alice”[2] in Moscow, defines his cooking style as a craft. He is known for creating the finest dishes from handcrafted ingredients, from bread to dressing. He is passionate for technology of the cooking process. As a result, his kitchen is original, deeply creative and meticulously thought out. This interview will lead you through Artem’s thought process in creating food and offer a fascinating behind-the-scenes glimpse at the craft of cooking which you will not see from the dining room.

[1]https://www.instagram.com/a.chy_

[2]https://www.instagram.com/alice_restaurant_msk.
“Alice" is a part of the gt. restaurant group founded by Elina (https://www.instagram.com/elina_tabidze) and Galaktion Tabidze (https://www.instagram.com/galktion_tabidze)

JUnQ: Can you elaborate on your concept? What is your approach in the kitchen?

Artem Chudnenko: To me cooking is a craft. It is the same kind of a craft as building a house or crafting a chair. Just like a carpenter starts with wood and cuts out a chair using a plane, making something great. A cook crafts in the kitchen: takes little pieces and makes one big great thing. One can be a good carpenter or an ordinary one. The good carpenter always tries to find ways to improve the chair, while the ordinary carpenter just routinely makes an ordinary chair. And I want to be the good one in my profession. So, I put effort in improving things: not only when creating food, but also when I communicate with the guests or journalists.

Now, what is there to improve in the kitchen? Here is a figurative example. When you cook pasta, it can turn out tasty or not: it can be undercooked or overcooked, with too much salt or too little salt. These are measurable parameters. So, if one can get all these right, one can say “I can cook pasta”. Next, there is room for improvement: for example, you can add butter or add oil, or seasoning. In the end, it is no longer plain pasta but a decent meal. In the concept of crafting, you can also make pasta yourself, which brings the final product on a qualitatively different level. In fact, you can handmake many things.

For example, we decided against purchasing commercially available miso pasta and bacon. Instead, we develop our own ingredients which we can make ourselves from raw materials, that is essentially everything from bread to soy sauce. We make our own garum (ancient Roman fish sauce) from langoustine, beef and scallops. It is indeed more complicated for the kitchen, but it is also cheaper and, in a sense, more sustainable. Because we utilize the ingredients that would normally not go into a dish, i.e. the scallop muscles, veins, shells etc. Recently we started making our own butter which goes so well with our own bread. Soon, we will substitute the commercial sunflower oil with fermented beef fat.

So, this is my approach in a nutshell and the concept of our restaurant “Alice”. I am trying to see to what extent we can go away from buying things towards handmaking them. And I think this is what makes our restaurant so special as compared to others.

JUnQ: The topic of our issue is serendipity, which happens to be a scientist’s best friend. How is it in culinary? Have you had serendipitous discoveries in the kitchen? Have you ever stumbled onto something great accidentally?

Artem Chudnenko: I think I am yet to create something truly great. One of my favourite discoveries is substituting coffee with roasted barley which grew koji on. At some point I needed coffee for a sauce for duck. But I had troubles describing to a barista what flavour of acidity, I exactly needed. It was my intuition that luckily helped me realize that roasted barley resembles coffee. So, I dried it and made coffee, it was perfect for the sauce.

Another great and interesting thing came out as a result of a collaboration with another chef from Saint Petersburg. I had an idea of a desert called “bread, not yet bread, no longer bread”. Basically, it was going to be an ice cream made from sourdough, covered with crunches of malted bread, and on top of all, yesterday’s bread was meant to be re-used for some sort of sweet cream. For the latter, the plan was to soak yesterday’s bread in beer, add honey, dried fruits etc. and mesh it up into a creamy mass.

It was so very tasty in my head and so easy to make. However, while the other components turned out well, the sourdough ice cream was problematic. I expected to get something light, resembling sour cream. But in reality, I did not get anything other than plain raw dough - opposite of tasty. In the end, we just left this mass, what was meant to become the sourdough ice cream, in a fridge for a week. After some time, we noticed that the mix started to separate into whey and curds. We helped it further with a blender and as a result obtained very nice butter, a little sour, due the sourdough. Now, we have our own butter in the restaurant. Furthermore, we figured out how to make use of the leftover liquid whey: we evaporate it until it becomes very dense and viscous. Something like condensed milk, but very salty and sour, and at the same time caramel and milky like. So, we pour this onto the butter, while the butter will be unsalted. Thus, it is sort of a closed cycled bread ecosystem: we serve the butter with the bread, the butter is made from the sourdough and the whey is a by-product of making the butter, but we then add it again to the butter.

There is also a truly serendipitous discovery. There was time when biodynamical approaches in the kitchen were very popular, in particular, lacto-fermentation, that is the process that produces traditional dill pickles or sauerkraut. In Russia, among other fermented delights at that time, lacto-fermented plum was at the top of the list. To be honest, back then I could not understand its taste – it felt like biting with its sweet-sour flavour. One day, I was to cook venison with carrots and a beetroot sauce, and plum seemed to me a good fit there. And I thought it would need to be a lacto-fermented plum. I asked my sous chef to ferment the plum. Since she was a somewhat younger cook, all this lacto-fermentation hype went past her and she didn’t know what I was asking for. Luckily, there was a similar process we used for making what I call a mushroom soy sauce. I make minced mushrooms, salt them and put the mass aside. After some time, this mix gives out sour juice and the left-over press cake we leave unused. This sour juice is quite tasty, I boil it down to further saturate the flavour. In the end it becomes a scrumptious mushroom sauce.

Figure 1. Scallop ceviche with fermented plum tiger’s milk.

So, I said to my sous chef: “Nastja, let’s do with the plum the same as we do for mushroom sauce, but instead of the liquid we will use the plum itself”. For some reason I trusted her and it wasn’t until shortly before the dinner when we realized that she had mixed all up. I was furious at first because there was no time to redo it. When I cooled down and tried the juice she had made, I immediately realized what other dish to prepare with it. It decided to soak the spices which I think all go into the tiger’s milk. That is a traditional citrus-based, spicy marinade used to cure fish in classic Peruvian ceviche.[1] This aggressive citric acid causes the proteins to denaturate thus the seafood appears cooked. It must be prepared fresh and consumed immediately, some also drink the sauce, so it is very much liked.
So, we did the same with our plum sour juice, added a little bit of seaweed broth to fine tune the acidity for the scallop to not be overcured in the acid. And the final dish, the scallop ceviche with fermented plum tiger’s milk, is still one of the top choices on our menu (Fig. 1).

JUnQ: Are all dishes a derivative of some other dishes with slightly different ingredients or can there be truly original dishes?

Artem Chudnenko: This issue is nicely discussed in the book “You and I eat the same” by René Redzepi. It says that in every place on Earth, there was the same kind of “bread” developed at some point in time. Be it pita or taco, in the essence it is still bread. And there was always something to go along with this “bread”, e.g. butter, guacamole, hummus, salo etc. In that sense, I think, since the appearance of bread, we no longer create anything conceptually novel. That was such a revolutionary transformation - from seeds to bread.

This however does not interfere with originality. Especially nowadays, when we can see how things are made on the other end of the world. For example, in our restaurant we have tabbouleh from quinoa with langoustines (Fig. 2). Tabbouleh is an appetiser originally coming from Syria. It is usually made from bulgur or kus-kus. And I, a russian guy, decided to make tabbouleh from South American quinoa, feature it with Japanese shitaki mushrooms and mix everything with chopped langoustines. There is no such dish anywhere in the world, but the style of the dish, its genre, if you wish, was there way before me.

Another interesting example is the cake “Anna Pavlova”.[2] It was named after a prima ballerina from Mariinsky theater, but the homeland of this dessert is still not decided between Australia and the New Zeeland.[3] Essentially it is a meringue-based cake topped with berries and whipped cream. Now, imagine I make the cream with feijoa and the meringue from bay leaves, it will still be Pavlova. Or if instead of berries I add berry ice cream, it will also be Pavlova.

There are, however, examples of absolute crazy innovations. Albert Adriá,[4] a chef of the restaurant El Bulli in Spain, who is known for his wondrous, surprising and delicious ideas, created transparent bread.[5] Another example is the creation of Grant Achatz,[6] the chef of three Michelin Star restaurant Alinea in Chicago. In that restaurant you could try an edible balloon made from green apple taffy filled with helium.

JUnQ: What is your creation process?

Artem Chudnenko: It starts with a defined task: say we need to develop our own miso pasta. First thing I do is the literature search to see what and how it has been done before. Then I try things out in the kitchen, which often do not work out the first time I try. For example, it took us half a year to work out the way to make the perfect miso pasta for our needs. At first, the taste was off, then it was too liquid. In fact, only recently I figured out a way how to make it of the right consistency. On top of it, it takes ca. 1.5 month for miso pasta to mature. So, it is very long until you can get a feedback.

The same story with bacon. As follows from our concept, buying bacon is not an option, also our kitchen equipment does not allow us to make bacon ourselves. So, I was to come up with a suitable substitution to use for breakfasts. In the meantime, I had a collaboration with another chef. The idea was to cook a steak as follows: let the meat soak in koji for four days, let it dry for one day, then fry and finally bake overnight. In the end, that “steak” turned out to be a wonderful pastrami-like meat. And that was it! Similar technology is now used in our restaurant to make a good substitution for bacon for our breakfasts.

Figure 2. Tabbouleh from quinoa with langoustines.

Finally, we need to “compose” a dish using individually optimized ingredients. For this step, we keep track of everything what is going on by using some sort of run sheets stating the ratio of the components. For example, here is the recipe of a dish based on our crafted bacon and brioche:

1. beef breast - 50 gr
2. egg - 1 pc
3. brioche - 50 gr
4. avocado cream - 20 gr
5. hollandaise sauce - 20 gr
6. fresh chives - 2 gr
7. black pepper - 1 gr

I will strictly follow the numbers in this recipe and try what comes out of these numbers. I will then intuitively know whether it has too much or too little of something, so that I can adjust the numbers. Or if one of the ingredients is off, so that I will need to figure out what else would suit here. In the end, the routine goes like this: cook - try - adjust - try again.

Also, interesting and puzzling is that when I work out larger volumes, simple scaling up does not work. Say, if I need to prepare ten times the amount of the aforementioned bacon with brioche, if I just take ten times as many ingredients, it will taste differently as compared to the small test portion. And usually, it is the amount of salt that needs to be adjusted.

JUnQ: Your approach sounds quite scientific. Yet, in science there are parameters which can be measured compared to one another (e.g. voltage, energy, density) while in culinary there is taste which seems a subjective measure. How do you deal with it?

Artem Chudnenko: Let's turn to music for an analogy, and let's disentangle, say, the technical part (the performance) and the content (the notes, the rhythm). So, the latter, the selection of notes played is obvious (also personal): either you like it or not. And the technical part can be measured. A false note is false for everybody. Nobody perceives it as, say, a unique signature of an artist. Otherwise, newbies would all have these signatures. Then, if the rhythm is off, this can be measured too. Nobody likes to listen to a cacophony, even those without any training.

The same in culinary: there is somebody who does not like the combination of, say, cauliflower with tahini (that's personal). Or let's rather take a steak as an example. You can dislike the sauce that goes along with the steak: it can be too sour or too sweet. But the steak itself can be either good - you took good quality meet and cooked it as it was requested (rare/medium/well done), or bad - if you overcooked/undercooked it or simply didn't do it the way your guest had asked for. And finally, the quality of the raw product is something that can be evaluated in our craft as well.

JUnQ: Related to music is another interesting question. It is well known that Ludwig van Beethoven suffered from deafness especially in the last decades of his life, but he continued to compose. Do you think there could be a chef without nose?

Artem Chudnenko: Absolutely. There is an interesting example of the aforementioned Grant Achatz. In 2007, he was diagnosed with tongue cancer and he lost the ability to taste anything at all. He had to trust his sous chefs for their sense of taste. He would write everything down what they were describing, then tell them what to change and then over again. I cannot imagine how weird it is for a chef to not discern any flavour at all. Luckily, he is fine and cancer-free now.

JUnQ: You mentioned that intuition helps you compose, how do you develop an intuition? Do you just eat a lot?

Artem Chudnenko: I think I eat a lot. As in any other case, the intuition in the kitchen is developed by constantly trying things out. When we are kids, we are naive, but as we grow older and mature, we gain experience and learn based on this empirical knowledge. Say, you once walked on the ice, slipped and broke your arm, and next time you know that you should not do it the same way again. At some point you already have enough experience to extrapolate it to alike situations and anticipate the outcome.

Similarly in food, but here, these basic categories are flavours or textures: sweet, salty, soft, crunchy, puree-like etc. You try mixing and learn that generally sweet and sour works well together. Or that having something crunchy in a dish almost always feels good. Quite often I go to other restaurants and I try out new combinations in my kitchen too. Sometimes I happen to have two random things on my spoon. And when I try, I realize they turn out to combine pretty well. I remember this combination, so that in the future my intuition strikes me to employ this combination in a dish.

For example, once I was in the restaurant "Kagges" in Stockholm where I tried baked cabbage with red caviar and sour cream. This is in my experience a very standard mix. But that sour cream was seasoned with lavender, which was an unexpectedly fine combination. Then I realized that this kind of flowerish flavour, even perfume-like, can go very well with caviar. It appeared handy, when for the New Year in "Alice", we were to make pancake tartlets with caviar. Obviously, caviar should go with butter and the butter, in turn, needs some seasoning. I remembered the positive experience and so I was looking for something flowery to add. It turned out that the zest of sour lemons, that we used for another dish, yielded exactly this perfume-ish flavour I needed.

JUnQ: Does cooking need everyday practice and refinement of the skills?

Artem Chudnenko: Absolutely. I spend a lot of time in the kitchen, that is why I still can control the cooking process perfectly. I know, there are chefs who indulge in creating new dishes and may lose some basic cooking skills, like, for example, when it comes to chopping something quickly etc. I, on the other hand, enjoy the time spent in the kitchen very much, and I am absolutely into frying, chopping etc. So everyday practice in cooking is important too. But the creation skill also needs practice. Generally, I try to work out 2-3 dishes a week, of which 1-2 may end up on the menu. Thus, we monthly have 1-2 new items on the menu.

JUnQ: In one of his interviews, Alain Ducasse said that being a great cook is 95 percent hard work and five percent talent, do you agree? Is there anything else one needs?

Artem Chudnenko: Alex Atala, a Brazilian chef, once said that the most important thing is to accept the routine. It is in fact true that every step in a career of a chef is more or less routine. When you just come to work in the kitchen you are given absolutely routinely stuff to do, like a robot. When I started, I was to cut cabbage all days long, or peal gazillions of potatoes, not even cooking it. Then you get promoted to actually cooking but it is again the same things over and over again. One day you cook puree and the other day you cook another kind of puree, and on the third day it is again the first puree. And when you become a chef, you also follow a routine but of a different kind. More poetic, perhaps, and what, I think, applies to every kind of craft is expressed perfectly in the words by Mike Sheenoda (Linkin Park):
"This is ten percent luck, twenty percent skill
Fifteen percent concentrated power of will
Five percent pleasure, fifty percent pain"

JUnQ: Thank you very much for the interview!

— Mariia Filianina

Read more:

[1] https://en.wikipedia.org/wiki/Ceviche.
[2] https://en.wikipedia.org/wiki/Pavlova_(cake).
[3] H. Leach, *The Pavlova Story: A Slice of New Zealand's Culinary History*, **2008**, Otago University Press.
[4] https://en.wikipedia.org/wiki/Ferran_Adrià.
[5] http://www.gastronomytime.com/crystal-clear-bread-from-albert-adria/.
[6] https://en.wikipedia.org/wiki/Grant_Achatz.
[7] https://en.wikipedia.org/wiki/Alex_Atala.

“You didn’t expect that?!” - Survey

Kevin Machel

Every now and then we find ourselves being puzzled by the unexpected. Of course that can sometimes be entertaining as in a good movie, book or video game. But when it happens out of the ordinary it might also have serious implications as in medicine or science. See what surprised our readers:

“I was unexpectedly diagnosed with having what is called “cold nodules” in my thyroid. It happened as we were training how to do a thyroid sonification-screening with patients as a part of an ENT (ear-nose-throat)-course in my 6^{th} semester in university. I volunteered to play the role of a patient for my peers. A peer then sonicated my thyroid and was a bit puzzled by seeing something odd. He found several small low echo nodules. The doctor in charge of our group sent me to the radiologist to do a scintigraphy right away. They then found that it were so called “cold nodules”. That means spots that are less active then the surrounding thyroid-tissue. These are the better nodules that you can have. Since then I have them controlled every year and I have to take an iodine supplement as a precautionary step. This emphasizes doing a check-up once in a while, who knows what one might find. In academic research, it might be nice to find something but in medicine, you rather don’t want to find anything out of the ordinary.”

Gina, 23, medical student

“In my opinion, serendipity is greatly reduced by a combination of inefficient student management, haste and mediocrity. Nowadays, every Ph.D is in a hurry. Four years may look like a lot of time at the beginning of a Ph.D but inefficient student and project management make it fly by fast. What to do when you’re stuck in a project that doesn’t get you anywhere? You, as a Ph.D to be, start ringing the bell, right? This is what’s expected of you, once you have your Ph.D. We are not just handing out Ph.Ds for doing some lab work getting data. Students that don’t figure this out by themselves need to be better managed, encouraged, or in the worst case, if the Ph.D seed doesn’t grow, let go. If you find yourself in a nice project and it’s all going well and your data is looking promising the clock still never stops. During this sprint to the finish there is little time to look at that funny data you got when you were just trying things or when it was not going very well, even if it actually might be something interesting. Sometimes there’s no motivation or desire anymore! Yes, I’ve seen demotivated students being stuck because they didn’t ring that bell in time. The end of your Ph.D - and the contract - is always just around the corner.
One thing I remember from a Ph.D. project: the student was sitting opposite of me in my office. The project didn’t show what they wanted, they found, as far as I remember, that a sample on a substrate still behaved as if it had water in between the sample and the substrate although none should have been present. When I heard this I asked about it. “This is a nice project for the next Ph.D” was the answer. I don’t think it has been pursued yet. Another thing is what I noticed myself on a single crystal ice boule. Made from the same water, in the same way, by the same ‘machine’ as all the other ones. Even after weeks in the same fridge under the same conditions the boule had a whitish surface while all the other ones were crystal clear. We don’t know why that happened. The milky boule has evaporated.”

Anonymous

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.

Non-Coding Sequences - the Dark Matter of Biology

Tobias Ruff

A couple of phenomena in cosmology (for example the speed at which stars move around the center of galaxies) contradict predictions made based on the amount and properties of the observable matter in the Universe. These phenomena indicate that there is something besides the matter we can observe with (radio-) telescopes, which is therefore called "dark matter". Physicists consider the question about the nature of this dark matter one of the most fundamental unsolved questions, because the amount of dark matter required to explain the phenomena is higher than the amount of "conventional" matter observed in our Universe.[1]

In biology, there is also a phenomenon which is not well understood in detail and which is maybe equally surprising: there are long parts of DNA for which there is no known function. These parts are sometimes seen as an equivalent of dark matter in biology:[2] it is known that they exist, but their function is unknown. The fact that the sequence of the human genome[3] and that of many other organisms is known, does unfortunately not mean that we understand the function of all parts of the genome. Investigating the role of certain genes or parts of the genome is actually an important part of molecular biology research.

Studying the effects of altered variants of a certain stretch of DNA is a possible approach to learn more about the function of the corresponding stretch of DNA. From an evolutionary point of view, there are sometimes surprisingly little effects in animals with a defect gene: Mice without functional prion proteins show no pronounced deficits.[4]

The same is true for mice without a functional form the the so-called amyloid-precursor protein (APP).[5] The function of the two corresponding genes is not well understood, although the aggregation of prion proteins is the cause of bovine-sponge encephalopathy (BSE) and the aggregation of APP cleavage products a possible cause of Alzheimer's disease.

Mutations in DNA sequences with vital function are lethal for a cell. A cell could for example not live without components for the generation of energy. The genes encoding for these components are therefore highly conserved across a wide range of species. In contrast, DNA sequences without any function for an organism can accumulate random mutations over many generations without affecting the survival or the reproduction of an organism. Stretches of DNA with a high degree of variability across species and even within individuals of a certain species are therefore usually assumed to be "junk DNA", i.e. DNA without any obvious function for an organism.

Another reason why they are assumed to be without function is the fact that they often consist of many repetitions of one sequence. Their content of information seen from a theoretical point of view is therefore low. The number of repetitions in certain parts of the DNA is even very specific for certain individuals and their relatives making them useful for the identification of individuals and their relationship to each other. The repetitive nature of large parts of the DNA provided early evidence about their origin: viruses are basically stretches of DNA or RNA enclosed by proteins and have the ability to replicate inside a cell. In some cases, these stretches have the ability to integrate themselves into the genome of its host cell. In case these events occur multiple times, the genome of a cell will contain multiple copies of the viral sequence.[6] With the accumulation of mutations in these sequences of viral origin across generations, they lost the ability to act as templates for the production of viral proteins and silently remained inside the genome of the host species.

However, the transcription to RNA and eventually the translation to protein are not the only functions a stretch of DNA can have. Controlling how much of a certain protein gets produced at a given point in time is at least as important as the information about the sequence of the protein itself. This gets obvious if one takes into account that the genome of a cell in the liver is identical to the genome of a neuron, although these cells look entirely different and also fullfill very different functions. Beyond the parts directly in front of a given protein-coding region the three-dimensional arrangement of the DNA inside a cell is also likely to influence how accessible certain parts of the DNA are for the production of proteins. How DNA with the long non-coding parts is spatially arranged inside the nucleus of a cell is an intriguing, but also difficult question to examine. Even if one could resolve the arrangement of the DNA strand inside the nucleus with (electron) microscopy, one could still not tell what the sequence of the visible part of DNA is. What seems to be clear so far is the existence of certain defined arrangements of the DNA which are not random.

Read more:

[1] Frieman, J. A. et al. (2008). Dark Energy and the Accelerating Universe. Annual Review of Astronomy and Astrophysics 46(1), 385-432.

[2] http://en.wikipedia.org/wiki/Biological_dark_matter

[3] International Human Genome Sequencing Consortium (2001), Initial sequencing and analysis of the human genome. Nature, 409(6822), 860-921.

[4] Büeler, H. et al. (1992). Normal development and behaviour of mice lacking the neuronal cell-surface PrP protein. Nature, 356(6370), 577-582.

[5] Zheng, H. et al. (1995). β-Amyloid precursor protein-deficient mice show reactive gliosis and decreased locomotor activity. Cell, 81(4), 525-531.

[6] Bourque, G. et al. (2018). Ten things you should know about transposable elements. Genome Biol 19, 199.

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