Science Focus 科言

Issue 019, 2021

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Message from the Editor-in-Chief 主編的話

Dear Readers,

Welcome to the latest issue of *Science Focus*. Many of us may be relieved for the passing of 2020, a year when our in-person interaction with colleagues and students has been dramatically reduced. Learning at home with online material requires tremendous discipline and self-motivation. These are also qualities that many successful scientists possess. Therefore, hold on to the good learning habits you have developed – they may be useful for years to come.

Working in relative isolation is not a new phenomenon. In this issue, we bring you the story of Grigory Perelman, who worked in solitude for years to crack one of the biggest problems in mathematics. We also hear from Ivan Ip and Julie Semmelhack, on their more sociable journey to faculty positions at the HKUST. For those of you looking for scientific inspirations and curiosities around you, we bring you stories of the one-eyed sheep, beer froth, garlic breath and DNA that can be passed between bacteria. Last but not least, we take a closer look at the black hole, beyond its first image that was released in 2019.

As always, please visit our Facebook and Instagram pages, which are frequently updated. Specific to this issue, you will find additional coverage of Ivan's and Julie's interviews online. Finally, I wish you all a successful 2021.

Yours faithfully,
Prof. Ho Yi Mak
Editor-in-Chief

親愛的讀者：

歡迎閱讀最新一期《科言》。不少人可能會為 2020 年的完結而鬆一口氣，因為在 2020 年我們與同事或是同學親身見面的機會並不多。利用網上教材在家學習對自律和積極性的要求極高，而這些都是不少成功科學家所擁有的特質。所以，請繼續保持您在這段時間得來的良好學習習慣，它們可能會對未來的您有用。

在相對孤獨的環境下工作並不是一件新鮮事，今期我們會向您訴說 Grigory Perelman 的故事，看看他如何花上數年時間獨個兒解構數學界其中一條最大的難題。另一方面，我們亦會聽聽葉智皓教授和 Julie Semmelhack 教授成為科大一員的歷程，他們的經歷中卻不乏與別人合作和交流的一環。對於喜愛從生活中找到啟發和趣味的您，我們特意準備了許多有趣的科學故事，包括關於能在細菌間傳遞的 DNA、單眼綿羊、啤酒泡沫和大蒜味口氣的文章。我們更會以 2019 年首次公開的黑洞照片作引子，向您進一步介紹與黑洞相關的知識。

跟以往一樣，我們鼓勵大家瀏覽我們的 Facebook 和 Instagram 專頁，那裡會有最新的科學資訊和小故事。您也可以在《科言》的網頁上找到今期兩位教授的完整專訪。最後，我祝您們有一個美滿的 2021 年。

主編 麥晧怡教授
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What's Happening in Hong Kong? 香港科技活動

Fun in Spring Science Activities 春日科學好節目

Any plans for this Spring? Check out these science activities!
計劃好這個春天的好去處了嗎？不妨考慮以下活動！

Conservation Laboratory – Unlocking the Secrets of Artefact Conservation
文物修復實驗室 — 透視文物修復的內裏乾坤

Date: Now – February 17, 2021
Venue: G/F Exhibition Hall, Hong Kong Science Museum

Remarks: No extra fee is required for museum visitors of Permanent Exhibitions. The Science Museum may be temporarily closed due to the latest social distancing measures.

展期：即日至 2021 年 2 月 17 日
地點：香港科學館地下展覽廳

備註：常設展覽廳參觀人士不另收費；科學館可能因應最新的防疫措施而暫停開放。

Did you know that artefact restoration requires the marriage of traditional Chinese craft techniques and advanced technology? The Hong Kong Science Museum has kept the "Conservation Laboratory", a part of the exhibition "The Hong Kong Jockey Club Series: Unlocking the Secrets – The Science of Conservation at The Palace Museum" in 2019. Visitors can understand more about the scientific principles and advanced analytical techniques behind artefact conservation through a series of interactive exhibits and models.

有沒有想過現代的文物修復工作原來需要傳統技藝和先進科技相輔相成才能達至盡善盡美？香港科學館把 2019 年舉辦的「香港賽馬會呈獻系列：內裏乾坤 - 故宮文物修復展」中的「文物修復實驗室」保留，讓參觀人士可以透過互動展品和模型了解與文物修復相關的科學知識和檢測技術，一嘗成為文物修復專家的感覺。

Robots – The 500-Year Quest to Make Machines Human
機械人的五百年

People started to design automatons since the 16th century. With advances in technology, these machines were used to replace human to perform repetitive tasks, which was essential to the Industrial Revolution. The robots nowadays have a humanized appearance and can imitate various human behaviors, such as walking, jumping and smiling. The latest AI technology even allows robots to think and learn.

In the near future, robots may have an unprecedented role in the society. What expectations should we have for them? The exhibition "Robots – The 500-Year Quest to Make Machines Human" will introduce you the 500-year history of the development of robots, and explore what they mean to us from the artistic and scientific aspects.

在 16 世紀，人們開始製造會自動運作的機械裝置。隨著技術的進步，這些機械裝置取代我們進行不少重覆性的工作，更是工業革命中不可或缺的元素。現代的機械裝置甚至有著人性化的外型，能做出人類的各種行為，例如走路、跳躍及微笑等；最新的人工智能技術更令機械人能思考和學習。

機械人未來也許會在社會上擔當著一個前所未有的角色，我們又應該有著怎樣的憧憬呢？「機械人的五百年」展覽會向您介紹機械人過去 500 年的發展史，亦會從藝術和科學角度探討機械人對我們的意義。

Date: Now – April 14, 2021
Venue: Special Exhibition Hall, Hong Kong Science Museum / online virtual tour

Extra fee is required for this special exhibition. The Science Museum may be temporarily closed due to the latest social distancing measures, but an online virtual tour is available free of charge for this exhibition (see the QR code).

展期：即日至 2021 年 4 月 14 日
地點：香港科學館特備展覽廳／網上虛擬導覽

備註：特備展覽需額外收費；科學館可能因應最新的防疫措施而暫停開放，但科學館亦為本展覽提供免費網上虛擬導覽（見二維碼）。

Before the Froth Fades Away:
Beer Froth and Its Mathematics
泡沫消失之前：啤酒泡沫的數學

By Ranting Huang 黃冉婷

You are in a bar trying to get some beer. The bartender comes and serves you a large glass of Guinness. The dark caramel colored liquid pours into the glass, producing a large head of foam. Before the froth fades away, you take a good sip of the beer, feeling completely invigorated.

Arnd Leike, a physicist from Ludwig Maximilian University of Munich focusing on renewable energies and particle physics, drinks too, but he gets more than just that. In 2002, Leike won the Ig Nobel Prize for demonstrating that the volume of beer froth obeys the mathematical law of exponential decay. The Nobel Laureate in chemistry, Dudley Herschbach, awarded him the prize at Sanders Theater, Harvard University. During the ceremony, Leike was given some beer served in a graduated cylinder, which was exactly what he used in his experiment.

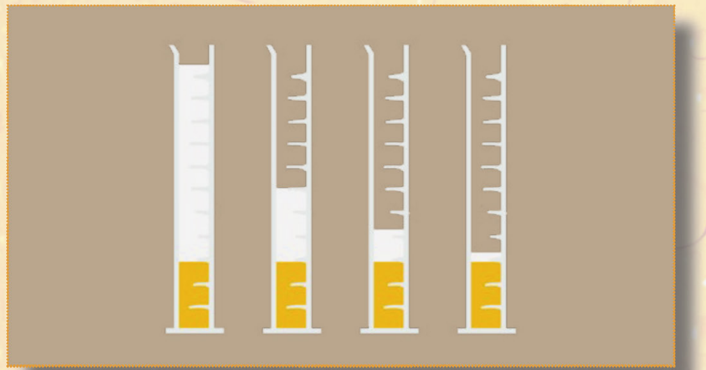
The initial goal of the research is to show his students how to check the consistency of theoretical models with experimental data. In the experiment, Leike used 3 types of beer – Erdinger Weissbier, Augustinerbräu München and Budweiser Budvar. For data collection, a graduated cylinder is filled with a freshly opened bottle of beer and the height of the froth is measured 15 times over a period of six minutes [1]. Later analysis of the data suggested that the rate of decay not only is exponential but also depends on the type of beer and can be used to differentiate beers [2].

The mathematical idea here is exponential decay. We say that a quantity is subject to exponential decay if it decreases at a rate proportional to its value. This phenomenon can be expressed in a simple differential equation, which is later showed to be an even simpler function, $y = ae^{-bt}$. Imagine a curve bending downwards with its tail going infinitely close to zero yet never reaching zero, and this is a simple graph of exponential decay. Mathematically, such a concise formula enables us to master complex physical systems in the sense that we can predict their futures as well as altering them.

Exponential decay, and exponential growth, are all around us. From a rapidly growing bacterial population to compound interest in finance, from Newton's law of cooling to variation in atmospheric pressure with altitude, this mathematical formula lies behind many phenomena on Earth. One of the scenarios where exponential decay applies is radiocarbon dating in archeology. With the law of decay known, half-life of carbon-14 can be deduced, and archeologists use this knowledge to estimate the age of fossils and other organic materials, such as bone and wood.

The story of the beer froth is not over yet. After Leike's publication, studies of the beer froth have continued. A research team from the University of Bremen, "called in question the results presented by Leike", stating that the foam volume does not follow a simple exponential law and includes more complicated factors [3]. And it is these clashes of thoughts that help sciences to advance like a never-stopping wheel. People study what was done before, learn from the successes and failures, and derive new ideas.

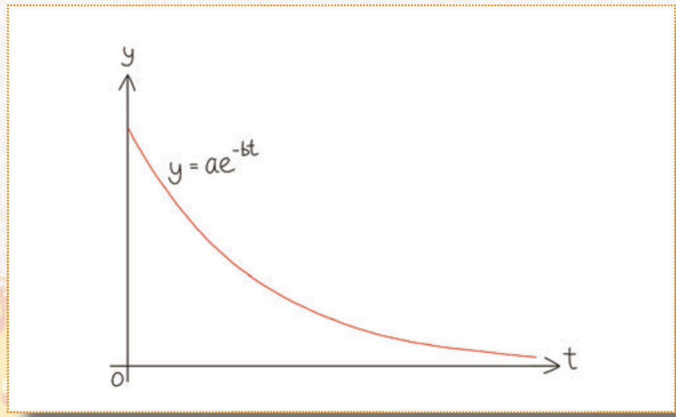
One may say that the Ig Nobel Prize should not be recognized in the same way as other prestigious prizes, yet just as the event's organizer Marc Abrahams said, "Every winner was chosen for work that first makes people laugh and then makes people think." [4]



設想你在酒吧，正打算來點啤酒喝。酒保給你上了一大杯健力士，你看著深焦糖色的液體被傾倒在杯子裡，激起了好些泡沫。在泡沫消失之前，你啜了一口，不禁感到神清氣爽。

路德維希 - 馬克西米利安 - 慕尼黑大學的物理學家 Arnd Leike 專注於研究可再生能源和粒子物理，他也喝酒，但並未止步於喝酒。2002 年，Leike 因為證明了啤酒泡沫的消散符合指數衰減規律而獲得搞笑諾貝爾獎。諾貝爾化學獎得主 Dudley Herschbach 在哈佛大學桑德斯劇院授予了 Leike 這一獎項。在頒獎典禮上，Leike 還喝到了裝在量筒裡的啤酒，而量筒正是他在實驗中使用的器材。

這項研究最初的目標是向他的學生展示如何檢查理論模型與實驗資料的一致性。Leike 使用了三種啤酒來進行實驗，分別是 Erdinger Weissbier、Augustinerbräu München 和 Budweiser Budvar。在收集資料的階段，剛開瓶的啤酒會被倒進標有刻度的量筒，並在六分鐘內分 15 次測量啤酒泡沫的高度 [1]。後來針對資料的分析表明，啤酒泡沫的消散速率不僅是指數級的(exponential)，還會因啤酒的類型不同而有所分別，而這一點恰好可用於區分啤酒 [2]。



這裡所涉及到的數學概念是指數衰減。如果某一個量的衰減速度和它的值成一定比例，我們則稱之為指數衰減。這種現象可以用一條簡單的微分方程表示，而稍加計算就可以得到一個更簡單的函數：$y = ae^{-bt}$。想像一條向下彎的曲線，其尾部無限接近於零，這便是表示指數衰減的圖像。從數學上講，這樣一個簡潔的公式使我們能夠掌握複雜的物理系統，進而可以預測它們的未來並對其進行改動。

指數衰減和指數增長無處不在。從快速增長的細菌種群到金融學裡的複利息，從牛頓的冷卻定律到大氣壓力隨高度的變化，指數變化隱藏在地球上許多現象的背後。指數衰減的例子之一是考古學中的放射性碳定年法。在知道了衰減的規律後，我們就可以推算出碳-14 的半衰期，考古學家則利用這些資訊來推算化石和其他例如骨頭和木頭等有機物的年齡。

啤酒泡沫的故事尚未結束。在 Leike 的論文發表後，相關的研究仍在繼續。不來梅大學的一個研究團隊對 Leike 的研究結果表示質疑，他們指出啤酒泡沫的消散並不僅僅遵循簡單的指數規律，而是包含了更複雜的因素 [3]。正因為有了這些思想碰撞的火花，科學才能像永不停息的輪子一樣前進。人們研究前人的成果，從他們的成功和失敗中學習，催生出新的想法。

也許有人會說，搞笑諾貝爾獎不應該與其他正經獎項一樣被嚴肅對待，但正如它的籌辦者 Marc Abrahams 所言：「每個獎項都是頒發給那些乍看之下令人發笑，繼而卻能引人深思的研究。」 [4]

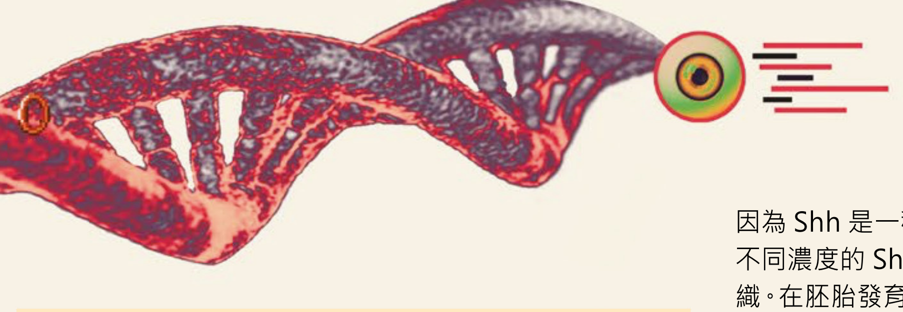
References 參考資料：

[1] Physicsworld. (2002). Beer paper wins Ig Nobel physics prize. Retrieved from *https://physicsworld.com/a/beer-paper-wins-ig-nobel-physics-prize/*

[2] Leike, A. (2001). Demonstration of the exponential decay law using beer froth. *European Journal of Physics, 23*, 21-26.

[3] Sauerbrei, S., Haß, E. C., & Plath, P. J. (2006). The Apollonian decay of beer foam bubble size distribution and the lattices of young diagrams and their correlated mixing functions. *Discrete Dynamics in Nature and Society, 2006*, 1-35.

[4] Nadis, S. (2002). Bubble won't burst for spoof Nobels. *Nature, 419*(6907), 549.



CYCLOPAMINE AND THE ONE-EYED SHEEP

環巴胺與單眼綿羊

By Kit Kan 簡迎曦

Most people consider one-eyed creatures like Mike Wazowski from the movie *Monster Inc.* and the cyclopes in Greek mythology to be fictional, because they have never seen animals like that in real life. Therefore, when sheep in the western United States gave birth to one-eyed lambs in the 1950s, the sheep ranchers freaked out. After decades of research, scientists finally identified the culprit that caused the disease and the underlying mechanism.

The singular eye deformity is caused by a compound called cyclopamine, which can be found in the plant *Veratrum californicum*. Ingestion of the plant at a certain stage during pregnancy hinders the development of the embryo – preventing the primitive, single "eye structure" from developing into two separate eyes, hence giving rise to only one eye. But how does a single molecule, cyclopamine, cause such great developmental changes? It all begins with a protein called sonic hedgehog.

Sonic Hedgehog and Cycloptic Sheep

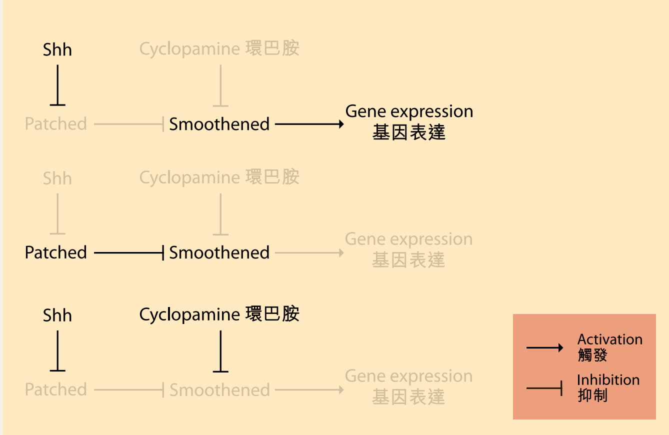
The sonic hedgehog protein (Shh) is encoded by the SHH gene and plays an essential role in embryonic development. Shh binds to a receptor on the cell membrane called Patched to inhibit it. Since Patched normally inhibits another protein named Smoothened, when Patched is inhibited by Shh, Smoothened is activated (double negative), which could lead to the expression of certain genes. The sonic hedgehog signaling is more complicated than that since it is a graded signaling pathway, meaning that cells exposed to different concentrations of the Shh respond in different ways, and will eventually differentiate into different tissues. In the early stages of development, there is a single structure called the eye field, which gives rise to two distinct eyes in the later stages with the help of the concentration gradient of Shh. Likewise, the left and right hemispheres of the brain are formed involving the same mechanism. Shh is not just responsible for the brain and eye development, but also the tooth, limb, and lung development.

Cyclopamine is an inhibitor of the sonic hedgehog signaling pathway. It has a very high affinity to Smoothened, binding it tightly and inhibiting it. Thus, even when Shh binds and inhibits Patched, Smoothened cannot execute its normal function of inducing gene expression [1]. If an ewe ingests the toxic plant and expose the embryo to cyclopamine at around day 14 of gestation [2], the brain and the eye field of the embryo will not separate, resulting in the deformity [3]. As mentioned previously, since the proper division of the two hemispheres of the brain also requires Shh protein [3], the cycloptic sheep not only has a deformed face, but also a deformed brain, which is why cyclopamine poisoning is potentially fatal.

From Fatal Poison to Cancer Therapy

The sonic hedgehog signaling pathway is also critical at later stages in life after embryonic development. Smoothened is a proto-oncogene while Patched is a tumor-suppressor gene. Tumor-suppressor genes, as the name implies, suppress the growth of tumor; and proto-oncogenes, when mutated, could contribute to the development of cancer. Basal cell carcinoma, the most common type of skin cancer, and medulloblastoma, the most common type of primary brain cancer in children, are some cancer types that result from mutations that over-activate Smoothened or inactivate Patched [4]. To deal with it, agents which can inhibit the activity of Smoothened (or Smoothened inhibitors) can potentially be used as drugs to slower cancer progression. Going from a fatal poison to a cancer therapy sounds too good to be true – although the cyclopamine derivative, saridegib, failed the clinical trial due to its unsatisfactory efficacy [5], it has inspired the birth of the two FDA-approved drugs, vismodegib and sonidegib, which are also Smoothened inhibitors [2]!

While you try to get the disturbing picture of the cycloptic sheep out of your mind, try to appreciate how innovative and creative scientists are, that they literally turn poison into medicine!



大多數人認為像電影《怪獸公司》中的「大眼仔」米高•華素基(Mike Wazowski)和希臘神話中的獨眼巨人這樣的單眼怪物都是虛構的，因為我們在現實生活中從未見過像這樣的生物。因此，當在1950年代美國西部有綿羊生下獨眼羔羊時，牧場的主人們都給嚇壞了。經過數十年的研究，科學家終於確定了導致該疾病的罪魁禍首及背後的生物學原理。

這種畸形單眼的現象是由一種名為環巴胺(cyclopamine)的化合物引起的，這種化合物可以在植物加州藜蘆(*Veratrum californicum*)中找到。在懷孕期間的某個階段攝入加州藜蘆會阻礙胚胎的發育，它阻止原始單一的眼睛結構分化成兩隻獨立的眼睛，從而只產生一隻眼睛。可是，環巴胺究竟是如何引起如此巨大的發育變化呢？這一切都始於一種叫做音速刺蝟(Sonic hedgehog/Shh)的蛋白質。

音速刺猬和單眼綿羊

音速刺蝟蛋白(Shh)由SHH基因編碼而成，在胚胎發育中扮演相當重要的角色。Shh會與在細胞膜上的稱為Patched的受體結合並抑制它。由於Patched通常會抑制另一種名為Smoothened的蛋白，因此當Shh抑制Patched時，Smoothened會被激活(雙重否定)，這能引發某些基因的表達。但Shh的訊息傳導並不是非黑即白的，因為Shh是一種分級的(graded)訊號，意味著細胞暴露於不同濃度的Shh下會有不同的反應，最終會分化為不同的組織。在胚胎發育的早期階段，只有一個稱為視場(eye field)的單一結構，該結構會在後期借助Shh的特定濃度發展出兩隻獨立的眼睛。同樣，大腦左右半球的形成亦涉及相同的原理。Shh不僅負責大腦和眼睛的發育，而且還負責牙齒，四肢和肺部的發育。

環巴胺是Shh訊息傳遞路徑的抑制劑，它能夠與Smoothened緊密結合並抑制它。因此，即使Shh結合並抑制Patched，Smoothened也無法發揮其誘導基因表達的正常功能[1]。如果母羊於妊娠的第14天左右攝入了帶毒性的加州藜蘆[2]，令胚胎接觸到環巴胺，胚胎的大腦和視場便不會分化成左右兩邊，從而導致畸形的情況[3]。如前所述，由於大腦兩個半球的適當劃分亦需要Shh蛋白[3]，因此單眼綿羊不僅臉部變形，大腦也會變形，這就是環巴胺中毒有可能致命的原因。

從致命毒藥到癌症治療

Shh訊息傳遞路徑在胚胎發育以後的人生階段也很關鍵。Smoothened是原癌基因(proto-oncogene)，而Patched是腫瘤抑制基因(tumor-suppressor gene)。顧名思義，腫瘤抑制基因可以抑制腫瘤的生長；而原癌基因在突變後，則可能有利於癌症的發展。基底細胞癌是最常見的皮膚癌類型，而髓母細胞瘤是兒童中最常見的原發性腦癌類型，這兩種癌症是一些因Smoothened和Patched突變而可能形成的癌症種類，當中通常是突變使Smoothened過度激活或使Patched失活[4]。為解決這個問題，使用抑制Smoothened活性的藥物(即Smoothened抑制劑)有可能減緩癌症進展。從致命毒藥變成癌症療法聽起來太不可思議 — 儘管環巴胺衍生物saridegib因療效欠佳而未能通過臨床試驗[5]，但它啟發了兩種FDA批准的藥物vismodegib和sonidegib的誕生(它們也是Smoothened抑制劑)[2]！

當你試圖從腦海中刪除那令人不安的單眼綿羊畫面時，也可嘗試欣賞科學家的創新精神和創意，因為他們確實將毒藥變成了抗癌藥物！

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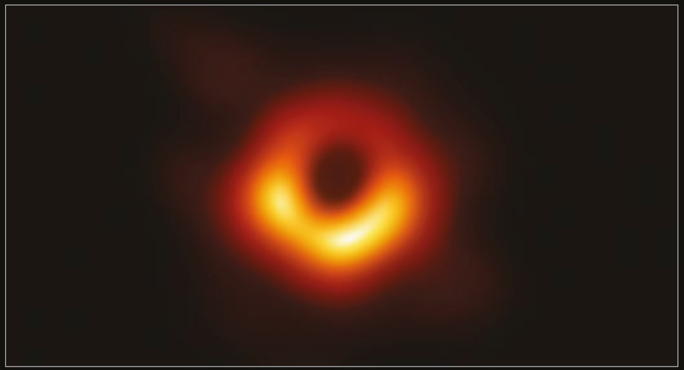
MythBusters: Black Holes
流言終結者：黑洞篇

By Sonia Choy 蔡蒨珩

On April 10, 2019, a team of scientists made history by capturing the first ever image of a black hole. This remarkable picture occupied headlines worldwide, and rightfully so – we never thought we would ever be able to capture a black hole in an image that can be passed around the world.

The black hole in question is a supermassive one, 2.4 billion times the mass of the Sun, at the center of the M87 galaxy, about 53 million light years from Earth.



The black hole at the center of the Messier 87 (M87) galaxy, in the constellation Virgo

Photo credit: Event Horizon Telescope Collaboration [1]

But first we have to answer the question – what exactly are black holes, and how are they formed?

Black Holes: A Brief Introduction

Although the existence of black holes was first speculated in the 18th century, they were first scientifically predicted by Einstein's theory of general relativity as a solution to the Einstein field equations. Einstein's theory of relativity can be elegantly summed up in twelve words from John Wheeler – "Space-time tells matter how to move; matter tells space-time how to curve [2]."

Mass bends the fabric of space-time itself; around a black hole's event horizon, the space-time is bent in a way that even light cannot escape. This occurs

when the size of a star collapses to a small enough size – more specifically, smaller than the Schwarzschild radius, $\frac{2GM}{c^2}$. (Here M is the mass of the star, c is the speed of light, and G is the gravitational constant.)

To put things into perspective, if the Sun were a black hole, it would have a radius of approximately 2.95 km; in comparison, the current radius of the Sun is 696,340 km. Actually, owing to the relatively tiny mass of the Sun, it can never turn into a black hole – so we won't have to worry about our Sun turning into a black hole any time soon!

The black holes we can see in the sky are formed by a process known as gravitational collapse. In a dying star, there is a reduction in internal pressure due to the fusing of heavier elements. As the internal pressure continues to decrease, gravity causes the star to further collapse onto itself. Eventually, the density of the star becomes high enough that it creates a very strong gravitational pull – and this is a black hole. You may recall the concept of escape velocity from high school physics; black holes are so small and massive that the escape velocity is greater than the speed of light. Nothing escapes a black hole – not even light.

And now a few myths:

Myth: This picture was taken by one telescope.
Busted.

This remarkable image was not taken by a single telescope, but rather an amalgam of images taken across eight telescopes on Earth known as the Event Horizon Telescope (EHT) [3]. To capture a reasonably clear image of an object so far from Earth, the telescope would require a very large aperture (the size of opening of the lens) to gather enough light from it. Instead of building one large telescope, the team decided that they would align the different EHT telescopes at the black hole at the same time, creating a large, "virtual" telescope. The aperture of this telescope becomes the distance between the two furthest telescopes – in this case nearly the diameter of the Earth! This vastly increases the resolution of the telescope and allows us to take images of objects that are far away. The image you see is an amalgam of data taken over eight sites in four days in April 2017 [4]; it was finally put together using techniques of image restoration to reconstruct a singular image from the large body of data.

Myth: Black holes only get bigger.
Busted!

One might think that black holes only swallow matter – this was what scholars had believed for a long time…until one day Mr. Hawking came along.

One of Prof. Hawking's greatest discoveries is Hawking radiation, a kind of radiation emitted by black holes. It is true that nothing escapes a black hole, but what was not known at the time was that they also emit radiation themselves [5]. The precise mechanism of its emission is difficult to state in full here, but the main idea is that due to quantum fluctuations, black holes are bound to lose energy, for instance, in the form of electromagnetic waves. If black holes emit more radiation than they absorb, then they will lose mass and eventually evaporate, due to the famous equation, $E = mc^2$, which tells us mass and energy are equivalent.

That being said, it will take a long time for black holes to evaporate and disappear: often we are talking about 10^{100} years, far, far older than the age of the universe (which is on the scale of 10^{10} years). Even the fastest-vanishing black holes vanish barely within the entire history of the universe, which is still a long time.

Myth: Black holes aren't black (since we can see them).
Busted.

Let's make it clear here, a black hole itself *is* pitch black – it is defined such that once anything goes beyond the event horizon, it cannot escape. What we can see in the image is the matter surrounding the black hole – a ring of matter and light that is about to disappear into the event horizon forever. The orange color you see in the photo, however, is artificially colored; it represents the intensity of radiation detected around the black hole, with the orange areas representing intense radiation and black representing areas with little to no radiation [4]. A black hole also emits Hawking radiation, as mentioned above, but this is so weak that we don't expect to be able to observe them in the foreseeable future.

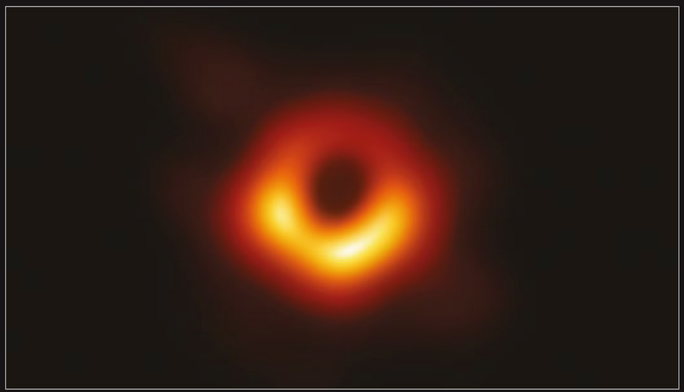
Myth: Once you fall into a black hole, you will be torn apart.
That is true.

This is due to a process known as spaghettification – caused by the gravitational gradient of a black hole. Due to a marked difference in strength of the gravitational field, gravity is stronger at your head than at your feet if you fall head-first into the black hole. This naturally causes you to be stretched vertically and compressed horizontally. These tidal forces are so strong that they can rip a person apart long before you reach the center of a black hole; chances are you will not survive the fall. *(Needless to say, the editorial team does not recommend falling into a black hole to verify this myth.)*

Side note: There is still so much to learn about black holes, but hopefully this article has piqued your interest. If you want to know more, the internet is filled with resources that will provide more information than this limited space. It's a good idea to learn something about Einstein's theory of relativity, since understanding black holes requires a good grasp of first special, then general relativity – good places to start include PBS Space Time and MinutePhysics (see the QR codes on P.9).

在 2019 年 4 月 10 日，一組科學家完成了壯舉：他們成功拍到了黑洞有史以來的第一幅照片。這張得來不易的照片理所當然地佔據了全世界報紙的頭版，畢竟人類從來也沒有想過自己能夠拍到黑洞，而且能夠把它廣傳。

照片中的黑洞是一個超大質量黑洞，質量是太陽的 24 億倍，位於離地球 5300 萬光年的 M87 星系中心。



處女座梅西爾 87（M87）星系中心的黑洞
相片來源：Event Horizon Telescope Collaboration [1]

首先我們要解答以下問題：到底黑洞是甚麼，又是怎樣形成的呢？

簡介黑洞

雖然科學家早於 18 世紀已經猜測到黑洞的存在，但最先在科學上預測到黑洞存在的卻是愛因斯坦的廣義相對論，那是作為愛因斯坦重力場方程式中的一個解。愛因斯坦的相對論大概可以用 John Wheeler 的一句話優雅地總結：「時空告訴物質怎樣移動，物質告訴時空怎樣扭曲（Space-time tells matter how to move; matter tells space-time how to curve）」[2]。

物質會令時空變得扭曲；在黑洞事件視界（event horizon）的周圍，時空扭曲得甚至連光也不能逃逸。這發生在一顆恆星塌縮至一定小的體積時，更準確地說，比史瓦西半徑（Schwarzschild radius）$\frac{2GM}{c^2}$ 還要小的時候（這裡 M 代表恆星的質量、c 是光速、G 是重力常數）。

讓我們從具體例子看看：如果我們的太陽是一個黑洞的話，它的半徑就會約為 2.95 公里；相比之下，太陽現時的半徑為 696,340 公里。事實上，因為太陽的質量相比下實在太微不足道了，所以我們永遠都不用擔心太陽會變成一個黑洞 — 這一定不會發生！

宇宙裡的黑洞都是從重力塌縮（gravitational collapse）的過程形成的。在一顆瀕死的恆星裡面，較重的元素會進行核聚變，令恆星的內部壓力降低；隨著恆星的壓力降低，引力會令它進一步塌縮，這星體的密度將會變得極高，所產生的重力也自然大得驚人 — 這就是黑洞。修讀高中物理的同學可能記得逃逸速度（escape velocity）這個概念：黑洞的體積極小、質量極大，令逃逸速度比光速還要快，所以沒有東西能逃出黑洞 — 連光也不能。

現在讓我們看看幾個流言：

流言：那張黑洞照片是由一座望遠鏡拍攝出來的。
流言破解。

那張了不起的照片並不是單憑一座望遠鏡拍攝出來的，它是由坐落於世界不同地方的八座望遠鏡拍攝得來的多張照片疊合而成，那八座望遠鏡被合稱為「事件視界望遠鏡（Event Horizon Telescope/EHT）」[3]。對於要拍攝這個離地球極遠的黑洞，如果要得出以令人滿意的相片質素，望遠鏡需要一個非常大的光圈（鏡頭開口的大小）來收集從黑洞發出的光。與其建立一座巨型的望遠鏡，研究團隊決定在同一時間把多座望遠鏡對準黑洞，創造出一座極大的「虛擬」望遠鏡。這座望遠鏡的光圈就變成了當中兩座相距最遠的望遠鏡之間的距離，也大概是接近地球的直徑！這大大提升了望遠鏡的解像度，使我們可以拍攝到很遠很遠的天體。你現在看到的影像是在 2017 年 4 月其中四天，從八個不同地方所收集的數據疊合而成的 [4]；它是由大量數據以影像修復技術重組而成的一張照片。

流言：黑洞只會越來越大。
流言破解！

你可能在想，黑洞只會吞噬物質 — 這也是科學家長久以來所相信的，直到一天霍金先生的來臨……

霍金教授其中一項最著名的發現是霍金輻射，也就是黑洞發出的一種輻射。的確，任何東西也不能逃出黑洞，但是當時的物理學家卻不知道黑洞本身也會釋放輻射 [5]。霍金輻射背後的理論難以在此詳細解釋，大概可說是因為量子漲落（quantum fluctuations）的關係，令黑洞傾向喪失能量，譬如是以電磁波（electromagnetic waves）的形式。如果黑洞發出的輻射比吸收的多，那麼黑洞的質量就會減少，最終會蒸發，因為 $E = mc^2$ 這條著名的方程式提醒我們：質量和能量是等價的。

雖說如此，黑洞要完全蒸發並消失的話，需要一段非常長的時間，所指的是以 10^{100} 年計的時間，因此宇宙的歷史（大概是 10^{10} 年的概念）相比之下只是九牛一毛。即使是最快消失的黑洞，消失的時間也很難短於宇宙至今的整段歷史，那相對上仍然是一段很長的時間。

流言：黑洞不是黑色的（因為我們能看見它）。
流言破解。

先要澄清一件事情，黑洞本身是 100% 黑色的，因為黑洞本身的定義為「任何越過了事件視界的東西一律都不能逃出黑洞」。我們在照片中看到的其實是圍繞著黑洞的物質 — 一環即將要消失在事件視界的物質和光。而在照片中看到的橙色是人工加上去的，它表示了黑洞附近的輻射強度：橙色部分代表較強的輻射，黑色部分則代表輻射較弱或沒有輻射的地方 [4]。如前文所述，黑洞本身也會發出霍金輻射，但由於強度實在太弱了，所以我們在可見將來也不見得能夠觀測到黑洞釋放的任何輻射。

流言：一旦掉進黑洞裡面，你的身體會被扯開。
流言證實。

這是因為一個稱為「意粉化（spaghettification）」的過程，它是由黑洞所產生的引力梯度所造成的。由於重力場強度的明顯差別，如果你是頭先掉進黑洞的話，你的頭所受的重力將會比腳所受的大得多。自然地，你的身體將會向垂直方向被拉長，向水平方向被壓縮，這些潮汐力（tidal forces）強得足以在一個人遠遠還未抵達黑洞中心之前就把他分屍，所以你跌進黑洞之後可以說是必死無疑。（*為安全起見，《科言》編採團隊並不建議你親身掉進黑洞來驗證這個流言。*）

後記：與黑洞相關的知識還有很多，希望這篇文章能令你對黑洞有更大的興趣吧！如果你想探索更多，網上有不少資源能提供更詳盡的資訊，比拙欄在有限空間內能提供的多。如果要對黑洞作更深入的了解，必須先學習愛因斯坦的相對論，首先是狹義相對論，然後是廣義相對論。值得介紹的包括以下兩個 YouTube 頻道：PBS Space Time 和 MinutePhysics。

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Photo Credits 相片來源：

The moon and the arc of the Milky Way: ESO/S. Guisard *(www.eso.org/~sguisard)*

Interacting Galaxies Group Arp 194: NASA, ESA, and the Hubble Heritage Team (STScI/AURA)

PBS Space Time

MinutePhysics

Garlic Breath...

and How to Deal With It?

蒜頭味口氣是……

By Kit Kan 簡迎曦

Have you ever had a dish containing garlic and had your mouth stinking for a very long time? You brushed your teeth several times and used the most minty mouthwash, but they all seemed to be useless. This article suggests a scientific approach to you to deal with garlic breath so that you will not embarrass yourself in future interviews or important events.

To tackle this problem, we have to first delve into the chemistry of garlic breath. The secret lies in the sixteenth element in the periodic table: sulfur (S). Garlic has many compounds that contain sulfur, such as allicin, allyl methyl sulfide, allyl mercaptan and diallyl disulfide. These are volatile compounds that give chopped garlic its distinctive pungent odor. After ingesting garlic, these volatile compounds would also evaporate in the person's breath, giving an unpleasant smell. Smelly sulfur compounds are not only found in garlics, in fact the nasty smell of farts and rotten eggs is due to the presence of hydrogen sulfide (H_2S)[1].

A combination of volatile sulfur compounds contributes to the distinct smell of garlic breath. While most of the sulfur-containing compounds found in garlic are metabolized relatively quickly, allyl methyl sulfide (AMS) is metabolized more slowly than the rest because an effective way to digest AMS is lacking in our body [1] and it can be detected in the breath for as long as 30 hours after ingestion of raw garlic [2]. The persistence of AMS is the reason why your breath still stinks the next morning after having garlic for dinner. AMS and other volatile organosulfur compounds are absorbed from the gut into the bloodstream and then expelled into expired air inside the lungs [1]. This is why brushing teeth and mouthwashes are ineffective in treating garlic breath.

Thankfully, there are a few effective ways for deodorizing a garlic breath situation. The first is to make use of specific raw foods to disable the production of smelly compounds in the body. In a study conducted by scientists in Ohio State University [3], it was found that raw foods high in polyphenols can reduce the amount of AMS in the breath after garlic

ingestion. Polyphenols are a group of antioxidant compounds present in plants and they can capture some organosulfur compounds and neutralize their odors to some extent. However, an enzyme called polyphenol oxidase can oxidize polyphenols into a more potent free radical form. The free radicals generated can effectively remove a stinky compound of garlic breath called allyl mercaptan, preventing it from being further metabolized by the body into its longer-living cousin AMS [3]. Common fruits high in polyphenols like apple, plum, cherry, peach and grape were all shown to have a deodorizing effect [4, 5], with apple's effect experimentally confirmed by data showing a reduction in AMS level [3]. Like most enzymes, polyphenol oxidase would become denatured at high temperatures, so it is most effective to eat your fruits raw and not cooked.

If you are not a fan of fruits, do not worry. Other studies have shown that drinking milk is also effective in treating garlic breath [6]. Volatile sulfur compounds can be classified into hydrophilic (water-loving) and hydrophobic (oil-loving) by their chemical structures. The concentrations of these compounds (including AMS) were shown to be reduced in the oral and nasal cavity after drinking milk. As milk consists of mainly water and a few percent of fat, it can dissolve both hydrophilic and hydrophobic organosulfur compounds and reduce their volatility. In addition, casein, a protein found in milk, was shown to be able to chemically react with disulfide compounds, such as diallyl disulfide. It has been postulated that diallyl disulfide can be metabolized into AMS through a reductive pathway with glutathione, a mild reducing agent used by our cells to reduce disulfide bonds [7]. Milk with its fat and casein contents can help to lower the amount of diallyl disulfide, a hydrophobic molecule, available to our system, and in turns less AMS will be formed. These can explain why drinking milk is a possible way to reduce garlic breath.

The next time you enjoy a slice of garlic bread, do not forget to have a glass of milk and an apple to go with it to prevent garlic breath and to make it a nutritious meal!

1 Remark: The myths and facts about farts were introduced in Issue 015.

您曾否試過因為吃了以蒜頭入饌的菜式，而令口腔在之後一段很長的時間都充斥著蒜頭的味道？儘管你已經刷了幾次牙，並用上最濃薄荷味的漱口水，但似乎並沒有甚麼作用。本文會從科學角度，提出一些方法處理蒜頭帶來的口氣，這樣你就不會在以後的面試或重要日子中因蒜頭味口氣而感到尷尬了。

解決問題之先，我們必須要了解蒜頭味口氣的化學原理。其秘密在於週期表中的第 16 個元素：硫(S)。蒜頭含有許多含硫的化合物，例如大蒜素(allicin)，烯丙基甲基硫醚(allyl methyl sulfide/AMS)，烯丙基硫醇(allyl mercaptan)和二烯丙基二硫(diallyl disulfide)等。這些都是揮發性化合物，使切碎的蒜頭具有獨特的刺激性氣味。進食蒜頭後，這些揮發性化合物會揮發至呼吸氣息中，散發出令人討厭的氣味。帶臭味的硫化物不單存在於蒜頭，事實上，屁和腐爛雞蛋的難聞氣味就是源於當中的硫化氫 (H_2S)[1]。

蒜頭味口氣的獨特味道由不同揮發性硫化物混合而成。雖然蒜頭中大多數硫化物的代謝都相對較快，但烯丙基甲基硫醚(AMS)的代謝速度卻比其餘的慢，這是因為我們體內缺乏有效分解 AMS 的途徑 [1]，因此進食生蒜頭後長達 30 小時，在呼吸中仍然可以檢測到 AMS [2]。長時間殘留的 AMS 就是為甚麼我們在晚餐吃了蒜頭後，口氣在第二天早上仍然久久不散的原因。AMS 和其他揮發性有機硫化物是從腸道被吸收到血液，然後排至肺部的呼出空氣中 [1]，這就是為甚麼刷牙和漱口水都無法有效去除蒜頭味口氣的原因。

幸好，有幾種有效的方法可以去除蒜頭帶來的口氣。第一是生吃某些特定食物來阻止體內產生帶有臭味的化合

物。在俄亥俄州立大學的一項研究中 [3]，科學家發現生吃含豐富多酚（polyphenols）的食物可以減少進食蒜頭後呼吸中 AMS 的含量。多酚是植物中其中一種抗氧化物，它們可以捕捉一些有機硫化物，並在某程度上中和它們的氣味。然而，多酚氧化酶可將多酚氧化為更有效的自由基形態，產生的自由基可有效去除蒜頭味口氣中稱為烯丙基硫醇（allyl mercaptan）的臭味化合物，防止其進一步被人體代謝成難以分解的「親戚」AMS [3]。蘋果、布冧、車厘子、桃和葡萄等富含多酚的常見水果均在研究中被發現具有除臭作用 [4, 5]，當中蘋果更在實驗中被證實能降低 AMS 水平 [3]。像大多數酶一樣，多酚氧化酶會在高溫下會變性，因此生吃未煮熟的水果是最有效的。

即使你不喜歡水果也不用擔心，其他研究表明，喝牛奶亦能有效對付蒜頭味口氣 [6]。揮發性硫化物的化學結構可分為親水性和疏水性（即親脂性）；研究發現在飲用牛奶後，這些化合物（包括 AMS）在口腔和鼻腔內的濃度都分別降低。由於牛奶主要由水和數個百分比的脂肪組成，它可以同時溶解親水性和疏水性的有機硫化物，從而降低其揮發性。此外，酪蛋白（casein），一種牛奶中的蛋白質，亦被證明能與二烯丙基二硫（diallyl disulfide）等的二硫化物發生化學反應。據推測，二烯丙基二硫可以在還原途徑（reductive pathway）中與麩胱甘肽（glutathione）被代謝成 AMS；當中麩胱甘肽是溫和的還原劑，能被我們的細胞用來還原二硫鍵 [7]。牛奶中的脂肪和酪蛋白可以減少體內可用的親脂分子二烯丙基二硫，從而減少 AMS 的形成。這些就是為何喝牛奶可以減少蒜頭味口氣的原因。

下次在享用蒜蓉包時，不妨配搭一杯牛奶和蘋果。這樣一來可以防止蒜頭味口氣，更可以使營養變得更豐富！

1 編按：第十五期《科言》內有更多關於屁的科學知識。

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A History of Plasmids: From Discovery to Application

質粒的歷史：從發現到應用

By Henry Lau 劉以軒

The world of life science is abuzz with exciting news all the time. Over the years, there have been golden rice and glowing mice, CRISPR and many more head-turning projects. It may surprise you that these curious biological wonders around the world owe their success to a teeny-tiny thing known as a plasmid.

One might say that modern biological research relies heavily on DNA technology. Ever since the confirmation of DNA as the "blueprint" of life and its characteristics were elucidated by many scientists over the years, DNA has become an integral part of life science research. Nowadays, scientists introduce foreign DNA as an extra set of commands into cell, to achieve all kinds of effects. The tool that has enabled all these is known as a plasmid. Next to the colossal coiled beast that is the bacterial chromosome, a plasmid is but an inconspicuous dot. It is a small stretch of DNA that serves as a vector. Think of it as an inbound car that takes the passenger, namely the foreign DNA, into another cell, by crossing the cell's borders, namely the cell membrane, so that the foreign DNA can perform its function inside the cell. While often overlooked, the plasmid's journey into the lab was nothing short of spectacular, combining not one but three important stories.

The first part of the trilogy began near the mid-20th century. First glimpsed in the 1940s, plasmids were stumbled upon by scientists who wished to discover why some traits could be passed on by non-chromosomal DNA structures [1]. In the beginning, various scientists gave these circular DNA entities different names such as "pangene" or "cytogene". It wasn't until 1952 that Lederberg coined the term "plasmid" [1], which has been used ever since. He defined it as a "hereditary extrachromosomal element". In simpler words, plasmids exist outside of the host's chromosome and can replicate themselves independently of the host genome. Despite its independence, upon cell division, plasmids can also be passed from parent cells to daughter cells, that's why it's called a "hereditary" element. That being said, plasmids are not always retained and can be lost after a certain number of cell divisions.

Soon after the coining of the term "plasmid", scientists were able to determine that plasmids could provide special abilities to their hosts, much like modular upgrades that allowed bacteria to survive better in extreme circumstances, although

their presence was not essential for the day-to-day activities of the cell. This discovery came from Japanese scientists who studied *Shigella* bacteria that could not be killed by multiple antibiotics [2]. They discovered that some plasmids, termed "R-factors" (R for Resistant), conferred anti-antibiotic abilities to their hosts, akin to giving the bacterial cells shields against antibiotics. In modern life science research, the presence of antibiotic resistance genes on the plasmids can be exploited because it provides a method for scientists to eliminate the unwanted bacteria which did not successfully take up the plasmids that carry the "passenger" gene(s) of interest.

The final breakthrough came in 1973, when the first artificial plasmid was constructed by Boyer and Cohen. By then, scientists had discovered that special proteins, known as restriction enzymes, could "cut" DNA by cleaving its intramolecular bonds. Particularly, Boyer has isolated a restriction enzyme, *Eco*RI[1], which could recognize and cut a particular sequence of DNA to produce unpaired DNA bases on one strand, known as "cohesive end" or "sticky end" *(Figure 1)* [3]. Armed with this knowledge, he attempted to make a cut in a circular piece of DNA to insert foreign DNA into it. This was, however, unsuccessful as the restriction enzyme cut his circular DNA in multiple locations, fragmenting it [4]. This setback was later remedied by Cohen, who met Boyer at a conference in 1972. Cohen shared with Boyer his plasmid, which the restriction enzyme would cut only at one precise location, and his method to introduce plasmids into bacteria [3, 4]. In this collaboration, they were able to insert a foreign piece of DNA into the plasmid and deliver the combined product into bacteria. This was the first instance of recombinant DNA where DNA from different sources were combined and made to proliferate inside cells, all thanks to the plasmid. Ever

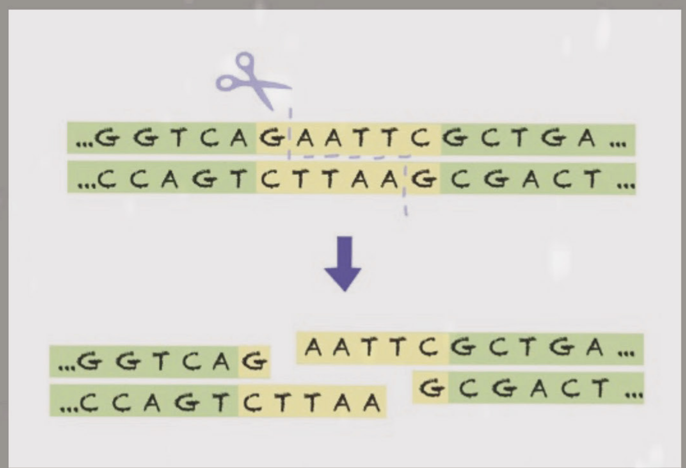

Figure 1. *The restriction enzyme EcoRI recognizes and cleaves the sequence "GAATTC" to produce cohesive ends.*
圖一 *限制酶 EcoRI 會辨認及切割「GAATTC」序列，並產生黏端。*

since Boyer and Cohen's success, plasmids have been an indispensable part of a life scientist's arsenal, performing previously difficult feats such as protein production or gene silencing.

This spectacular story of how plasmids became an essential research tool is, in fact, a culmination of stories from different parts of the world over a span of 21 years. Despite its unassuming size, the plasmid relied on the work of not one but many scientists to unlock its secrets, highlighting the collaborative nature in science.

1 *Eco*RI: It was named *Eco*RI because it was the first enzyme isolated from <u>*E*</u>*scherichia* <u>*co*</u>*li* strain <u>R</u>Y13.

在生命科學的世界裡時時刻刻都會出現令人振奮的消息。這些年來，極受注目的研究項目有很多，包括黃金大米、會發光的小鼠、CRISPR 等等。你可能會感到驚訝的是，原來這些生物學上的奇蹟背後都全靠一種細小至肉眼也看不到的東西 — 質粒（plasmid）。

你可以說現代生物學研究全賴基因編輯技術。自從脫氧核糖核酸（DNA）作為「生命藍圖」的角色得以證實，以及其特性在多年來被科學家清楚闡明後，DNA 成為了生命科學研究中不可或缺的一部分。現在，科學家會把外來 DNA 引入細胞作為一組額外的指令，做出各種各樣的效果，而使這一切變得可行的就是質粒。在像野獸般龐大的細菌染色體旁邊，質粒看起來只不過是一顆不顯眼的小點。它是一小段作為載體的 DNA：你可以想像它是一輛從境外駛來的車輛，而接載的「乘客」是外來 DNA，車輛穿越了一條名為細胞膜的「國界」，把外來 DNA 接載到另一個細胞內，讓它在裡面發揮作用。質粒成為實驗室「鎮室之寶」的故事雖然經常被人遺忘，但卻能使人讚歎。當中涉及不止一個，而是三個重要的故事。

三部曲中的第一部發生於 20 世紀中期。質粒在 1940 年代首次受到科學家關注，當時科學家希望解釋為甚麼一些性狀能經染色體以外的 DNA 結構遺傳下去，他們偶然發現了質粒 [1]。起初，不同科學家給這些環狀 DNA 結構取了不同的名字，例如「pangene（泛生子）」、「cytogene（細胞質基因）」等，直至 1952 年 Lederberg 才把它們命名為日後被廣泛使用的「plasmid（質粒）」[1]，並把其定義為「染色體外遺傳物質（hereditary extrachromosomal element）」。簡單來說，質粒存在於宿主的染色體外，具有獨立地自我複製的能力，而複製過程不受宿主基因組所限。雖然質粒是獨立於宿主本身的基因組，在細胞分裂時，它仍然能夠由母細胞被傳到子細胞，這是它被定義為「遺傳」物質的原因。雖說如此，質粒也未必能一代一代地永遠遺傳下去，而是可能在數次細胞分裂後丟失。

定下「質粒」這個名字之後不久，科學家發現它們能讓宿主得到一些特殊能力，就像附加了一些組件而被升級了一樣，使細菌可以更容易在極端環境下生存，儘管質粒對細胞的日常運作來說並不是必需的。這發現源於日本科學家，那時他們正在研究一些多種抗生素均不能殺死的志賀氏菌（*Shigella*）[2]，他們發現某類稱為「抗性因子（R-factors）」的質粒就像能為宿主提供對抗抗生素的盾牌一樣，讓宿主得到抗生素耐藥性。在現今的生命科學的研究中，質粒中的抗生素抗性基因可調派上用場，因為它提供了一個方法，讓科學家可以消滅那些沒有獲得質粒的細菌，從此篩去沒有攜帶著目標基因的細菌。

最後一個突破發生於 1973 年，Boyer 和 Cohen[1] 製造出第一顆人造質粒。當時，科學家已經發現了一些名為「限制酶」的特殊蛋白質，它們可以通過切斷 DNA 之間的鍵來切開 DNA。特別的是，Boyer 提取了一隻名為 *Eco*RI[2] 的限制酶，它可以辨認並切割某個特定的 DNA 序

列，使切割位置兩端內的其中一條 DNA 鏈帶有沒有配對的鹼基，產生「黏端（cohesive end 或 sticky end）」*（圖一）*[3]。利用這個發現，Boyer 嘗試在環狀 DNA 上進行切割並希望將外來 DNA 插入其中。然而這實驗卻以失敗告終，因為限制酶在多個位置切割他的那顆環狀 DNA，把它切得支離破碎 [4]。後來 Boyer 於 1972 年的一次會議上遇見了 Cohen，後者提供了解決這個難題的方法。Cohen 把他的質粒分享給 Boyer，那質粒的特別之處在於限制酶只會準確地在當中的一個位置進行切割。另外 Cohen 亦跟 Boyer 分享了他把質粒引入細菌的方法 [3, 4]。在這次合作中，他們成功把外來的 DNA 片段插入質粒，並將重組質粒送至細菌內。這是歷史上首次製造出重組 DNA，當中不同來源的 DNA 被併合在一起，並且能在細胞內進行自我複製 — 這些都要歸功於質粒。自 Boyer 和 Cohen 的成功以來，質粒一直是生物學家工具箱內一件不可或缺的工具，它使以前困難的工作，例如控制蛋白質合成或基因靜默（gene silencing）等都變得易如反掌。

質粒如何成為重要研究工具這個偉大故事，實際上，是由 21 年間發生在世界不同地方的小故事編織而成的。儘管質粒的大小毫不起眼，也需要很多科學家花上不少心血才能揭示當中的奧秘，過程中更凸顯了互相合作這個科學本質。

1 香港教科書中被翻譯為波耶（Boyer）和柯恩（Cohen）。

2 *Eco*RI：命名為*Eco*RI是因為它是從大腸桿菌（<u>*E*</u>*scherichia* <u>*co*</u>*li*）<u>R</u>Y13菌株中提取的第一種限制酶。

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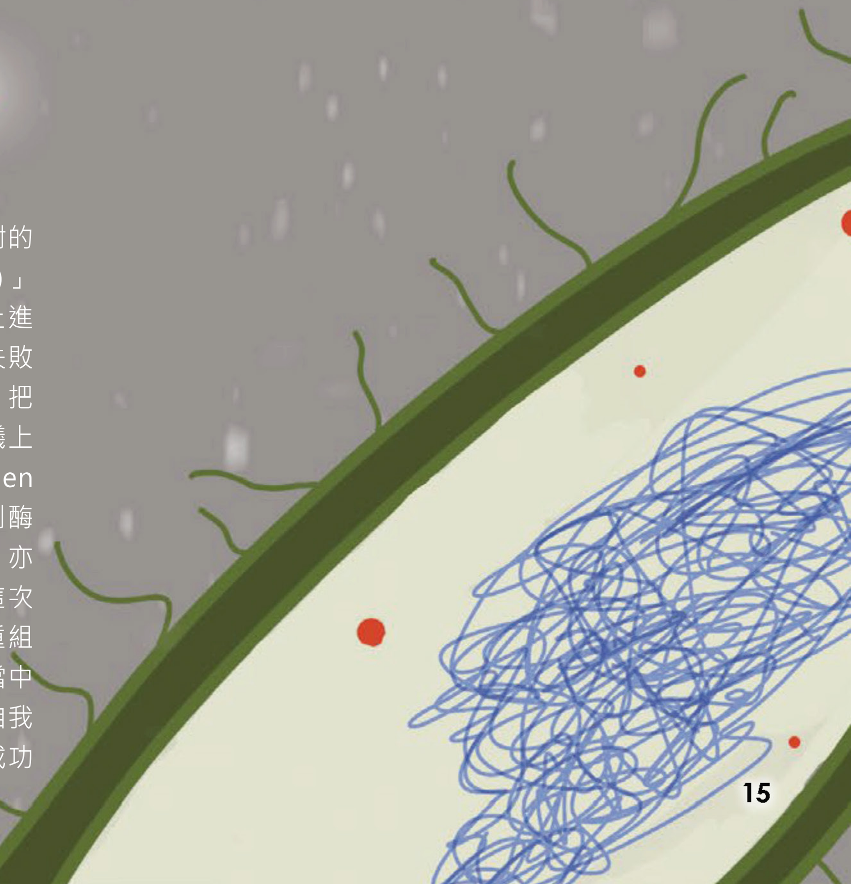
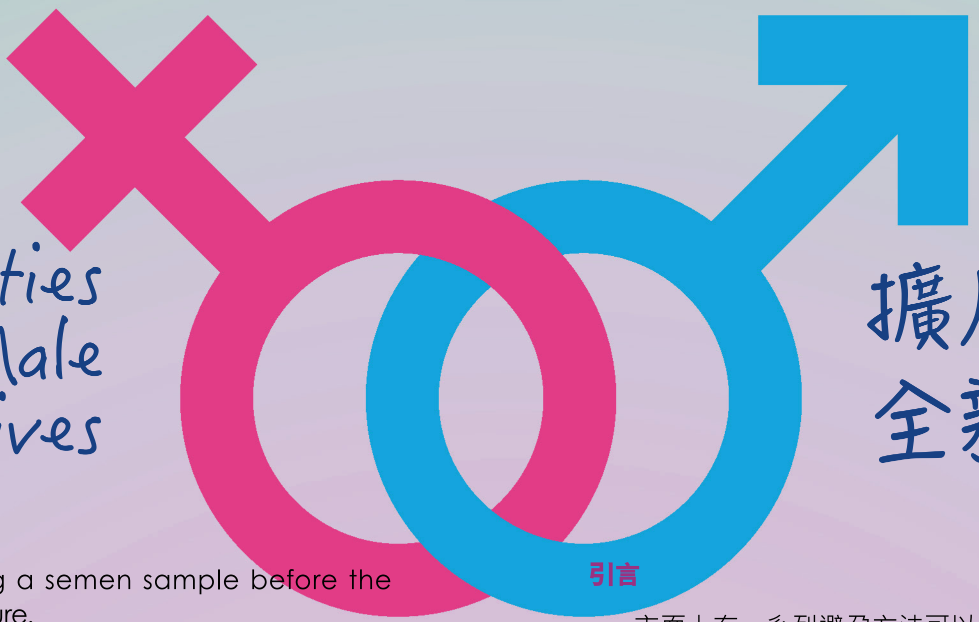


Extending Equal Opportunities to Contraception: Novel Male Contraceptives



擴展兩性平等：全新的男性避孕方法

By Clara Tung 董卓衡

Introduction

To prevent unintended pregnancies, a series of contraceptive methods could be used, such as condoms, female condoms, diaphragms, oral contraceptives, contraceptive patches[1], vaginal rings[2], intrauterine devices (IUD)[3], etc. The birth control approaches currently available largely targets the female side. Despite the fact that female contraceptives are very effective, they may have side effects and the use of those contraceptives is sometimes constrained by certain health conditions of women. With the increasing trend of gender equality in family planning, there is an urge for scientists to invent some novel male contraceptive methods.

Existing Male Contraceptive Methods

Four hundred years have passed since condom was first being used [1], but the variety of male contraceptive methods remain limited. Both of the effective contraceptive options for men nowadays, condoms and vasectomy, act as a physical barrier to prevent sperms from reaching the egg, which makes fertilization impossible.

Condom, usually made of latex, is an artificial barrier which can also prevent the transmission of sexually transmitted diseases (STDs), for example, syphilis and human immunodeficiency virus (HIV). Pregnancy rates of using condoms as the only contraception approach reaches 15–20% per year, mostly resulting from the improper or inconsistent usage, or breakage [2]. People who have latex allergy can choose the slightly inferior alternative, polyurethane condom, which has a higher breakage rate and slippage rate. It is, however, reported in a research study that polyurethane condom can provide better sensitivity to the male users [3].

On the other hand, vasectomy, a highly effective method with a failure rate of <1%, is a surgery under local anesthesia that severs the vasa deferentia (sperm ducts). Nevertheless, it cannot be regarded as a truly reversible method because even after the operation of vasectomy reversal, the pregnancy rates can only be restored to 50–75% [2]. For this reason, doctors may suggest freezing a semen sample before the contraceptive procedure.

Experimental Male Contraceptives

In response to the urge to develop new male contraceptives, some experimental approaches have been proposed, focusing on ways to inhibit sperm production by hormonal or non-hormonal methods. For such a male contraceptive to be considered practicable, the sperm count has to be reduced down to <1 million sperm per milliliter, statistically equivalent to a fertilization rate of <1% per year [2]. In addition, an ideal contraceptive should be free of side effects and administered by infrequent injections. The effect should also be reversible so that sperm production could resume after the discontinuation of treatment.

Hormonal Male Contraceptives

Female contraceptive pill contains estrogen and progesterone that inhibit follicle maturation and ovulation by lowering the levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secreted by the pituitary gland. This relies on the negative feedback between the two sets of hormones; high levels of estrogen and progesterone inhibit the secretion of LH and FSH. A similar relationship was also found in male between testosterone and progesterone, and LH and FSH; administration of testosterone and progestins (synthetic progestogen) can suppress LH and FSH secretion [2]. Low concentrations of LH and FSH prevent the testes from

引言

市面上有一系列避孕方法可以防止意外懷孕，例如男用避孕套、女用避孕套、子宮帽、口服避孕藥、避孕貼 [1]、陰道環 [2]、子宮環 [3] 等；可是現有的節育方法主要針對女性一方。儘管女性避孕方法非常有效，但它們可能帶來副作用，而且女性的某些健康狀況亦可能限制她們使用這些避孕方法。隨著人們在計劃生育上的男女平等意識日益增強，這使科學家有需要發明一些創新的男性避孕方法。

現有的男性避孕方法

雖然避孕套的發明距今已有 400 年歷史 [1]，但男性避孕方法的種類卻仍然非常有限。如今，有效的男性避孕手段有避孕套和輸精管切除術，兩者都是充當物理屏障使精子不能與卵子相遇，從而防止受精。

避孕套通常由乳膠製成，亦是一個可以防止性傳染病（例如梅毒和人類免疫缺乏病毒（human immunodeficiency virus/HIV）等）傳播的人造物理屏障。不過使用避孕套作為唯一避孕方法的懷孕率可高達每年 15–20%，這主要是由於使用不當、沒有恆常使用或是避孕套破損所致 [2]。對乳膠過敏的人可以選擇避孕效果稍遜一籌的聚氨酯安全套（polyurethane condom），它有著較高的破損率和滑移率；然而據一項研究指出，聚氨酯安全套可為男性使用者提供更好的觸感 [3]。

另一方面，輸精管切除術是在局部麻醉下將輸精管切斷及結紮的手術，這是一個失敗率低於 1% 的有效方法。然而，它被認為是一種不能真正逆轉的方法，因為即使完成輸精管復通手術後，懷孕率也只能恢復到 50–75% [2]。因此，醫生可能會建議在手術前先冷凍保留精液樣本。

試驗性的男性避孕藥

針對研發創新男性避孕方式的呼聲，科學家提出了一些試驗性的方案，它們主要是通過使用激素或非激素的方法來抑制精子的製造。對於這類男性避孕方法，精子數量必須被降至每毫升少於 100 萬個，才能被認為是切實可行的方法，這在統計上亦相等於每年少於 1% 的受精率 [2]。此外，理想的避孕方法應該沒有任何副作用和不需經常接受注射，效果也應該是能逆轉的，使精子的生產在停止療程後能得以恢復。

男性用的荷爾蒙避孕藥

女性避孕藥含有雌激素和孕酮，它們通過抑制腦下垂體分泌促黃體激素和促卵泡激素來抑制卵泡的成熟和排卵。這依賴於兩組激素之間的負回饋關係：高濃度的雌激素和孕酮會抑制促黃體激素和促卵泡激素的分泌。在男性中，睾酮和孕酮與促黃體激素和促卵泡激素之間也被發現有著類似的關係，服用睾酮和黃體製劑（合成孕酮）可以抑制黃體激素和促卵泡激素的分泌 [2]，被降低了的促黃體激素和促卵泡激素濃度會使睾丸收不到產生精子所需的適當信號。因此，睾酮和黃體製劑有望被用於避孕。

一些使用這個原理的候選藥物已經進入臨床試驗階段，其中一種含有睾酮和黃體製劑、能經皮膚吸收的凝膠在初期臨床試驗的結果能令人寄予厚望。與此同時，另一種名為「十一酸二甲雄酮（dimethandrolone undecanoate/DMAU）」的分子被發現有潛質作為「單劑（single-agent）」避孕藥，因為它可以同時與雄性激素（包括睾酮）和孕酮的受體結合並把其激活，因此該分子可以模仿這兩種激素帶來的避孕效果 [2]。

激素和一些小分子（例如維生素 A 酸）如何在體內發揮作用？

類固醇激素和維生素 A 酸能與一類名為核受體的特殊蛋白質結合，而核受體實際上是轉錄因子（transcription factors）。與激素結合後，核受體會被激活然後誘導引發某些基因的表達，這能進而對個體帶來整體性的影響（例如增加或抑制精子的生產等）。

因此，我們可以利用不同方法操縱這些過程，例如施用其他可以激活同一個受體的替代分子（藥理上稱為促效劑（agonist）），或是使用一些可以堵住受體的分子（拮抗劑（antagonist）），以達到我們的目的（例如抑制精子生產等）。

receiving a proper signal for sperm production. In light of this, testosterone and progestins can potentially be leveraged for contraceptive functions.

Some of such candidates have already entered clinical trials. A transdermal gel containing testosterone and a progestin seems promising at the initial stage of the clinical trial. Meanwhile, another molecule named dimethandrolone undecanoate (DMAU) was found to be a potential "single-agent" contraceptive, because it can bind to and activate the receptors of both androgens (including testosterone) and progesterone, so the molecule can mimic the contraceptive effects of the two hormones [2].

How do hormones and some small molecules (e.g. retinoic acid) exert their functions in our body?

Steroid hormones and retinoic acid bind to a special class of proteins called nuclear receptors, which are in fact transcription factors. Upon hormone binding, nuclear receptors are activated to induce the expression of certain genes. This can in turn affect the individual as a whole (e.g. enhance/inhibit sperm production).

Therefore, it is possible to manipulate a pathway, for example, by administering an alternative molecule that can activate the same receptor (pharmacologically called an agonist) or blocking the receptor with another molecule (antagonist), to achieve our purpose (e.g. inhibit sperm production).

Next-Generation Male Contraceptives

On the other hand, there are certain downsides of hormonal male contraceptives. Treatment with testosterone were shown to associate with various negative side effects, from mood changes (e.g. aggression) and decreased libido, to cardiac toxicity and liver damage [4]. For athletes, the use of testosterone and some steroids may lead to sports disqualification. Are there any alternatives?

It was discovered that the active metabolite of vitamin A, retinoic acid, is crucial to sperm production. There are three types (isoforms) of retinoic acid receptors (RAR), RARα, RARβ and RARγ, but proper sperm production is found to be related to only RARα. Therefore, drug candidates which can impede the binding of retinoic acid to RARα, i.e. RARα antagonists, could possibly be used as contraceptives.

Research data showed that a pan-RAR antagonist, BMS-189453, which can inhibit all three kinds of RAR, can induce infertility in male mice without affecting the testosterone level [4]. Fertility was fully restored after the cessation of drug treatment which lasted for as long as 16 weeks [4]. While these results preliminarily demonstrated the practicality and advantages of using RAR antagonists as contraceptives, the next step is to assess its efficacy on higher mammals, such as non-human primates, before conducting clinical trials on human. In addition, researchers are trying to screen for an RARα-selective antagonist which does not inhibit RARβ and RARγ, so as to prevent any possible side effects that might arise due to the interference in the normal functions of the irrelevant RARs.

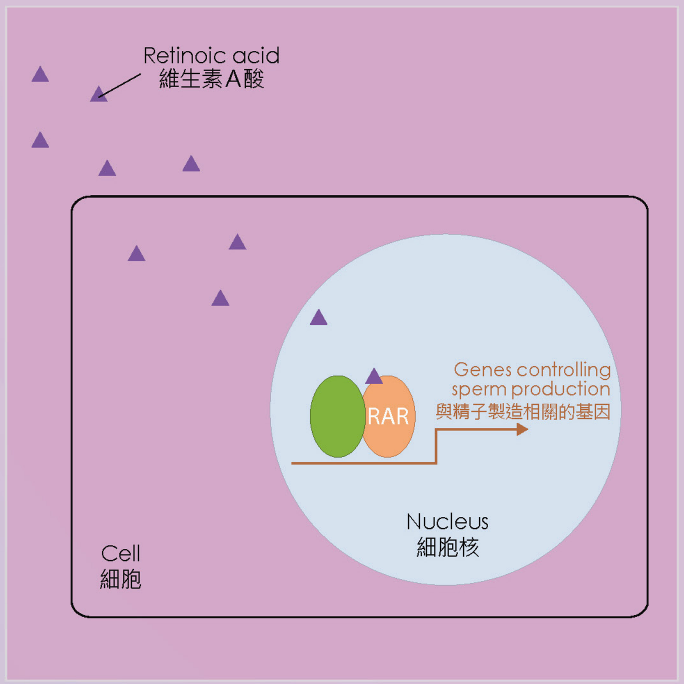
Conclusion

In the era of gender equality, it is preferable that both men and women can take an active role and share the responsibility in preventing unintended pregnancies by adopting contraception. As our understanding of the biology of our body develops through intensive research, novel contraceptive methods and drug candidates will probably arise. Novel male contraceptives are likely to present themselves in the market in the near future, providing alternatives for men beyond the two traditional methods. But until now, condoms and vasectomy are still the mainstream male contraceptive methods, especially condoms which can also prevent STDs.

1 Contraceptive patch: A sticky patch which prevents pregnancy by releasing estrogen and progestogen into the bloodstream via skin, mainly to prevent ovulation.

2 Vaginal ring: A small soft plastic ring which can be placed into the vagina by the user. It works by continuously releasing estrogen and progestogen into the bloodstream, mainly to prevent ovulation.

3 Intrauterine device (IUD): A plastic or copper device placed into the uterus by a doctor or nurse. It prevents pregnancy by releasing progestogen (plastic device) or copper (copper device) to alter the cervical mucus, so that sperm is less like to survive and reach an egg. Implantation of a fertilized egg can also be halted.



新一代男性避孕藥

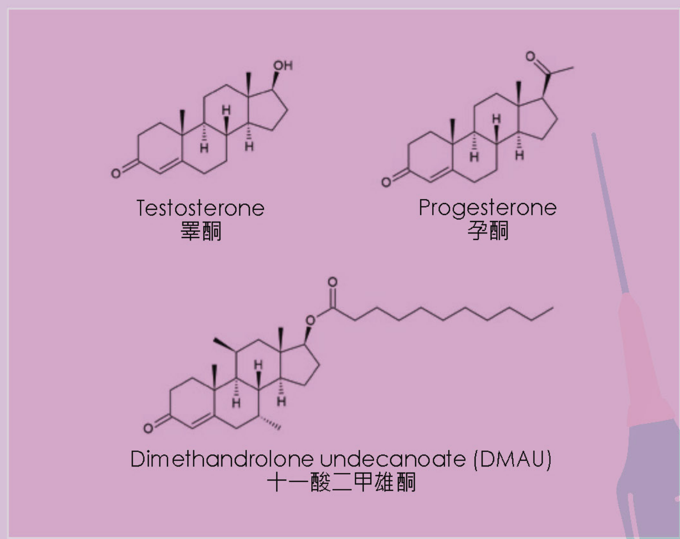
另一方面，荷爾蒙性男性避孕藥有著某些缺點。使用睪酮的療法被發現與多種不良副作用有關，例如由情緒變化(例如變得具攻擊性)和性慾降低，到對心臟有毒性和損害肝臟等 [4]。對於運動員而言，使用睪酮和某些類固醇更可能會導致他們失去比賽資格。那麼我們還有其他選擇嗎？

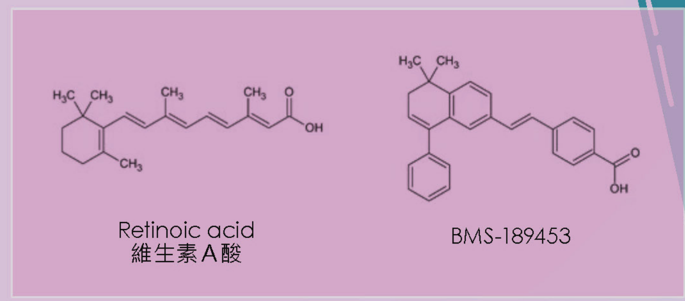
維生素A的活性代謝物 — 維生素A酸(retinoic acid，俗稱「A酸」)，被發現對製造精子至關重要。維生素A酸受體(retinoic acid receptor/RAR)共有三種同功型(isoforms)：RARα、RARβ 和 RARγ，但與正常精子生產有關的就只有 RARα。因此，可以阻礙維生素A酸與 RARα 結合的候選藥物 — 即 RARα 拮抗劑，則有望能被用作避孕藥。

研究數據表明一種可以抑制全部三種 RAR 的泛 RAR 拮抗劑 — BMS-189453，可以使雄鼠不育但不影響睪酮水平 [4]。在停止長達 16 週的藥物療程後，雄鼠的生育能力得以完全恢復 [4]。儘管這些研究結果初步證明了使用 RAR 拮抗劑作為避孕藥的可行性和優勢，但在對人類進行臨床試驗前，下一步先要評估的是它對高等哺乳動物(例如非人類靈長類動物)的功效。研究人員亦正在嘗試篩選出不會同時抑制 RARβ 和 RARγ 的 RARα 選擇性拮抗劑，以避免產生因為影響其他不相關 RAR 而帶來的任何潛在副作用。

結語

在兩性平等的時代，最理想的當然是不論男女都能積極地採取避孕措施和分擔避孕的責任。隨著研究不斷有所進展，我們對身體運作機制的認識也日益加深，嶄新的避孕方法和候選藥物可能會在未來湧現，全新的男性避孕方式也可能會在不久的將來投入市場，為男性提供上述兩種傳統避孕方法以外的替代方案。但直至現在，避孕套和輸精管切除術仍是男性避孕的主流方法，尤其是可以同時預防性病的避孕套。





1 避孕貼：一種可將雌激素和孕酮經皮膚釋放到血液的黏貼，避孕原理主要是防止排卵。

2 陰道環：一個可由使用者放入陰道內的細小軟塑料環，它能將雌激素和孕酮持續釋放到血液中，避孕原理也主要是防止排卵。

3 子宮環：一個由醫生或護士放入子宮內的塑料或銅製裝置。它通過釋放孕酮(塑料裝置)或銅(銅裝置)以改變子宮頸黏液的特性，使精子不易存活而無法到達卵子，受精卵也將不能植入子宮內膜。

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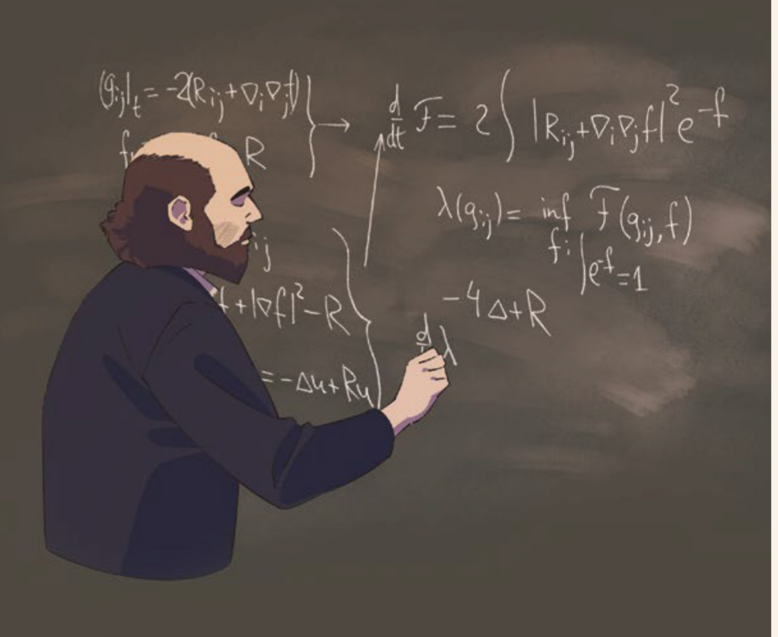
A Mysterious Maverick in Mathematics: Grigory Perelman

特立獨行的神秘數學家：Grigory Perelman

By Chun Ho Park 朴天浩



What are the values that a mathematician should hold at the highest standard? When Grigory Perelman refused an enormous prize for proving the Poincaré conjecture, he also proved that he did not value wealth and fame like others in academia. Just considering the fact that he refused the million-dollar prize and vanished from the mathematics community shortly after, you can see that he is one of a kind. Being the first and only mathematician to solve one of Clay Institute's Millennium Problems, his life story seems to be as mystifying as the million-dollar mystery he had deciphered.

So, what is the Poincaré conjecture, and why is it worth all the fuss? The Poincaré conjecture was one of the most prominent questions in topology, a subfield of mathematics concerned with the properties of special geometric objects. In topology, the shape of a doughnut is considered the same as that of a coffee cup, as one can be stretched and twisted to become the other, without cutting or making new holes in it. While the conjecture was very fundamental in nature and crucial in understanding the space we live in [1], it was notoriously difficult to prove, and many wrong proofs were submitted.

Born in Soviet Russia, home to many great mathematicians, Perelman had great passion for problem solving from a young age. While he was extremely talented in mathematics, he was also honest and careful to follow rules. Being a man of principle, mathematics had great appeal to him as one had to honestly follow established definitions and theorems to arrive at a logically-sound conclusion. Graduating with distinction from Leningrad State University and earning his PhD, he moved to the U.S. as he was invited to numerous research positions in prestigious universities. But, it wasn't until he had become infatuated with proving the Poincaré conjecture that he decided to leave everything behind and return to his home country to solely focus on this problem.

Before his eight-year commitment to proving the conjecture, he met Richard Hamilton, a mathematician at Cornell who had made significant progress in solving the problem by formulating a framework called the Ricci Flow [2]. In the hope of collaboration, Perelman wrote to Hamilton and shared his idea on how to solve this problem, but did not receive any reply. So, instead of collaborating with other scholars, he decided to tackle the problem in solitude, but built upon the works of mathematical giants like Thurston and Hamilton to solidify a complete proof. It was after five years of him working on the problem that the Clay Institute announced it as one of the Millennium Problems with a million-dollar prize. Although one could perceive this as a fortunate circumstance, nothing had changed for Perelman: he was only concerned with uncovering the truth.

After successfully proving the conjecture, he did not officially publish his results in a peer-reviewed journal, but merely posted it on the Internet as a preprint. It was as if he just wanted to let other mathematicians know of his discovery, rather than focusing on earning the credit for his astounding work. To explain his discovery, he accepted all the invitations from various institutes in the U.S., e.g. Princeton, Stony Brook and Columbia, to deliver lectures on his solution and answer everyone's questions about the proof. Not long after that, he won the Fields Medal and the prize from the Clay Institute, but refused both. The King of Spain attended the award ceremony, but Perelman was nowhere to be found. "It was completely irrelevant for me," Perelman remarked. "Everybody understood that if the proof is correct then no other recognition is needed." [3]

Intelligence, diligence, and persistence were certainly factors which allowed Perelman to succeed. But, his austere attitude towards mathematics was probably what allowed him to dedicate eight years of his life to solving one problem. This is what is most inspiring about his story: his firm belief on mathematics having to be purely about mathematics itself, nothing else. To quote Mikhail Gromov, one of Perelman's teachers, "To do great work, you have to have a pure mind. You can think only about mathematics. Everything else is human weakness. Accepting prizes is showing weakness." [3]

究竟一個數學家應該擁有怎樣的心態才算是達至最高境界呢？當 Grigory Perelman 婉拒了因證明龐加萊猜想（Poincaré conjecture）而得來的巨獎，他同時向世間證明了他並不為財富和名聲所動，這是在學術界鮮有的。單從他拒絕接受百萬大獎，以及不久後在數學界消聲匿跡的兩件事可以看到他是特立獨行的一個。作為第一位，亦是唯一一位成功解開其中一條克雷研究所千禧年難題的數學家，他的故事似乎比他對拒絕領獎一事的解釋更令人大惑不解。

那甚麼是龐加萊猜想？解開了龐加萊猜想為甚麼會令世界為之震驚？龐加萊猜想是拓撲學上其中一道最重要的問題，拓撲學是數學中一個關於特別幾何物件特性的分支。在拓撲學上，甜甜圈的形狀被視為與咖啡杯的一樣，因為兩者都可以透過被延展和扭曲變成對方，而不需要切割或從中製造新的孔洞。雖然這是本質上是十分基礎的一個猜想，對於理解我們身處的空間至關重要 [1]，可是它是一道著名的難題，使得數學家奉上不少未如理想的證明，鎩羽而歸。

Perelman 與不少偉大數學家一樣出生於蘇聯時期的俄羅斯，自小就熱衷於解決問題。在非常有數學天份的同時，他亦是一個誠實而且會小心翼翼遵循規矩行事的人。作為一個做事遵循原則的人，數學對他有一種特別的吸引力，因為那是需要從已確立的定義和理論，經嚴格邏輯推論後才能達至結論的一門學科。Perelman 在列寧格勒國立大學以優等成績畢業及取得博士學位後，因為受到不少著名大學邀請其從事研究職位而旅居美國，一直到他著迷於證明龐加萊猜想才決定放下在美國的一切回到老家，獨個兒專心鑽研這道難題。

在他開始花八年心力證明龐加萊猜想之前，他遇上過另一位康奈爾大學的數學家 Richard Hamilton，Hamilton 以往曾構想出一個叫「里奇流」（Ricci flow）的框架而在這個問題上推進了一大步 [2]。Perelman 一心想與 Hamilton 合作，因此寫了一封很長的信給他，信中把自己對於如何解決這道難題的見解分享給 Hamilton，可是最終並沒有收到任何的回覆。因此，他決定不與其他學者合作，獨個兒解決這個問題，但其實他並不算孤身上路，因為他是站在 Thurston 和 Hamilton 這些數學偉人的肩膀上，建基於他們的發現以架構自己完整的證明。在 Perelman 開始研究的五年後，克雷研究所才把龐加萊猜想列為千禧年難題，並懸賞 100 萬美元。換轉是其他人大概會對這筆可能飛來的橫財大嘆好運，但 Perelman 卻心如止水，因為對他而言一切都沒有改變：由此至終他只是想找出真相。

成功證明龐加萊猜想後，Perelman 並沒有把結果正式發表到經同儕評審（peer review）的學術期刊，只是在網上以預印本（preprint）的形式發表，就像他只想讓其他數學家了解到自己的發現一樣，而沒有想過要從自己的驚人發現中獲取任何榮譽。為了闡明自己的發現，他欣然接受了所有來自美國學術機構的邀請，包括普林斯頓大學、紐約州立大學石溪分校和哥倫比亞大學，到場講解自己的發現並逐一回答在場人士的問題。不久之後，他贏得了菲爾茲獎和由克雷研究所所頒發的獎項，但兩者都被他拒絕接受。西班牙國王也出席了頒獎典禮，卻未見 Perelman 的蹤影。「那個對我一點也不重要。」Perelman 評論道：「所有人都明白如果證明是正確就不需要額外的嘉許。」[3]

智慧、勤勉和堅持絕對是使 Perelman 成功的因素，但令他甘於奉獻八年時間去解答單一問題的原因要歸功於他對數學那樸素得稱得上為苦行的態度。這就是這個故事最具啟發性的地方：他在數學上的堅決信念只是單純地出於對數學本身，而不是別的東西。如果要引述 Perelman 恩師 Mikhail Gromov 的一句話，那就是：「要完成偉大的工作，你要有一顆純潔的心。你想的一切只可以關於數學，其他都是人性的弱點。接受獎項就是在暴露弱點。」[3]

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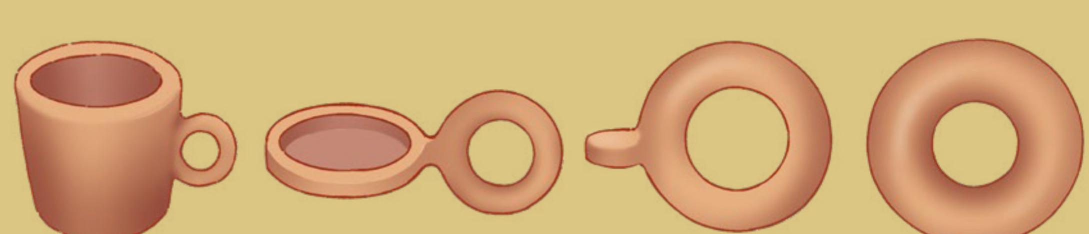

Q & A

WITH HKUST SCIENTISTS

科大科學家問答

By Sonia Choy 蔡蒨珩

In October 2017, Stephen Hawking allowed his PhD thesis *Properties of Expanding Universes* to be available online to the public, hoping to inspire others to think, learn and "look up at the stars and not down on their feet". It was accessed more than two million times within just a few days. We chatted with two scientists from different fields of science at HKUST to learn more about their favorite scientific work, inspiration and advice for students.

在 2017 年 10 月，Stephen Hawking（斯蒂芬霍金）在網上公開了他的博士論文 —〈宇宙膨脹的屬性〉，希望能夠啟發他人思考和學習。在短短幾天之內，論文已被閱讀超過 200 萬次。我們與科大兩位來自不同科學領域的科學家作專訪，了解他們最喜愛的科學研究、獲得的啟發及予學生的建議。

Professor Ivan Chi Ho IP
葉智皓教授
Assistant Professor, Department of Mathematics
數學系助理教授

Prof. Ivan Ip obtained his bachelor's degree from HKUST and PhD degree from Yale University. Before returning to HKUST as an Assistant Professor in 2018, he first served as a Project Researcher at Kavli IPMU, University of Tokyo, and then an Assistant Professor at Kyoto University.

葉智皓教授於科大取得其學士學位，並於耶魯大學取得博士學位。在 2018 年以助理教授身份回到科大之前，他先後於東京大學科維理宇宙物理學與數學研究所擔任項目研究員，以及在京都大學擔任助理教授。

Professor Julie SEMMELHACK
Julie SEMMELHACK 教授
Assistant Professor, Division of Life Science
生命科學部助理教授

Prof. Julie Semmelhack earned her bachelor's degree from Princeton University and PhD degree from University of California, San Diego. Before joining HKUST in 2017, she worked as a postdoctoral researcher at University of California, San Francisco and then Max Planck Institute for Neurobiology.

Julie SEMMELHACK 教授於普林斯頓大學取得其學士學位，並於加州大學聖地牙哥分校取得博士學位。她在 2017 年加入科大，此前她曾先後於加州大學舊金山分校和馬克斯•普朗克神經生物學研究所擔任博士後研究員。

1 Do you have a favorite piece of scientific work, or perhaps a particular scientist whose work you love?
您喜歡哪一份科學著作，又或是有沒有一位您喜歡其研究的科學家？

Prof. Ivan Ip : My favorite piece of work is Euclid's *Elements*. Euclid was a mathematician who lived around 300 BC, and many of the geometry results you learn in high school are based upon results in this book. It is probably the first ever mathematical work that uses strict, logical proofs; all the results and theorems in the books were derived logically from the five axioms at the beginning[1] that were assumed to be true. (The five axioms are things that just "make sense" as assumptions.) Euclid derived lots of results from them – for example, Pythagoras' theorem is #48 in the book, and was derived solely from the axioms and the previous 47 theorems.

It had a huge impact on me as a teenager, since in secondary school math, you only learn how to calculate, or just write two-line proofs in geometry – the sort of formal proofs seen in Euclid is almost never introduced in schools.

葉智皓教授：我最喜歡的作品是歐幾里得的《幾何原本》。歐幾里得是公元300年左右的一位數學家，現時在中學數學課學到的不少幾何定理也是基於這本書裡的結果。《幾何原本》大概是第一本用嚴密數學邏輯和證明寫成的數學作品，書裡的所有結果和定理都是從最初提出的五條公理[1]推論出來的。（那五條公理是一些「符合常理」的假設。）歐幾里得從公理推導出很多幾何定理，譬如說，畢氏定理就是書中第48條定理，他只用了五條公理和前面47條定理就成功把它推導出來。

《幾何原本》對中學時期的我有很大的影響，畢竟在中學數學課中涉獵到的大多都是計算，或是短短兩行的幾何證明，幾乎沒有提及《幾何原本》裡面那種正式的數學證明。

Prof. Julie Semmelhack : There are a couple of papers that influenced me. When I was applying for graduate school in 2001, I was a molecular biologist interested in neuroscience, but I wasn't sure if I could do both of these disciplines at the same time, since at the time it wasn't common. Then I read a paper about the study of memory using fruit flies, and the idea that something as abstract as memory could be studied using genetic tools seemed really cool and interesting.

Some mutant flies were lacking a certain gene, causing some parts of their mushroom body, the part of the brain involved in making memories, to be undeveloped. The idea was to do some genetic surgery to show that different parts of the mushroom body were involved in making short and long-term memories.

Julie Semmelhack教授：其實有幾份科學論文都對我帶來了影響。當我在2001年報讀研究院的時候，我從事的是分子生物學的研究，可是我亦對神經科學很有興趣。我不肯定自己可否同時從事這兩方面的研究，因為在當時這並不普遍。然後我看了一份在果蠅上研究記憶的論文，覺得即使是記憶那樣抽象的東西也可以用基因工具研究這一點很吸引和有趣。

有些突變果蠅缺乏了某一個特定基因，令參與腦部產生記憶的蕈形體（mushroom body）的某些部分發育不全。基本上就是要透過在這些果蠅上做一些基因手術，來證明蕈形體的不同部分分別參與產生短期和長期記憶。

2A How have you been inspired or intrigued by Euclid's *Elements*? How does it change your journey of science education and research?
《幾何原本》怎樣啟發或吸引著您？在科學上它對您的求學和研究生涯有著什麼影響？

Prof. Ivan Ip : This book had changed my impression of math as a subject – math became something extremely logical. There are no grey areas in math – if A implies B and B is false, then A must also be false – which is something unique to the subject. Literature is obviously extremely subjective, different economists might interpret the same set of data differently, and there are always errors in the sciences whenever you perform experiments. However, math has no room for any of that – if it is logically correct, then the result must be correct – it doesn't depend on whether you're the loudest person in the room. The book really influenced me in terms of choosing math as the subject I wanted to pursue in university.

This book also revealed to me that modern mathematics is far more than arithmetic, but proof and logic oriented. When we look back at *Elements*, Euclidean geometry is a topic we can draw by hand using diagrams, but when you turn the points and lines into variables and symbols, it is actually the precursor of abstract algebra. Everything concrete can be turned abstract, and this is what I am doing to this day, in my research on abstract algebra and representation theory – interpreting the geometric meaning as algebraic structures behind.

Also, an interesting little story here – I was quite naughty in secondary school, so on a school math exam, there were a few questions on the geometry of triangles – just very short proofs to prove that, for example, the triangles were congruent. After reading *Elements*, I tried writing the proof from scratch, starting from Euclid's axioms and deriving the results step by step. What required three lines ended up taking two pages! After that, my math teacher did tell me off, but he ended up giving me full marks on that question[2]. That's an example of math being right when it's logically sound – just that there are many methods to get there.

葉智皓教授：《幾何原本》改變了我對數學的看法 — 對我而言，數學從那時起變了一門極之講究邏輯的科目。數學裡沒有灰色地帶的存在；如果A意味著B，而B是不正確的話，那麼A一定也不正確。這一點跟其他學科不一樣，譬如說文學明顯是十分主觀的，不同經濟學家對同樣的數據可能會有不同的理解，就算是科學實驗也少不免會有誤差，但是數學就沒有這種不確定性：如果邏輯正確的話，結論也就必然正確 — 並不會因為你說話大聲就代表你是正確。這本書真的影響了我，令我在大學選擇修讀數學。

《幾何原本》也告訴我現代數學遠遠並不只是計算，而是講求證明和邏輯導向的。讓我們回到《幾何原本》，歐氏幾何其實是一門可以以畫圖表達的學問，但是如果我們把線和點換成變數和符號的話，那其實就是抽象代數（abstract algebra）的前身。任何實在的物件都可以化為抽象，這就是我直至現在也在做的，關於抽象代數和表現理論（representation theory）的研究，基本上是把幾何意義理解為背後的代數結構。

這裡說一個有趣的小故事吧：我在中學的時候也挺頑皮的，在一次學校數學考試中有幾條跟三角形相關的幾何問題，當中只要求一些簡單的證明，例如證明它們是全等之類；在看完《幾何原本》後，我嘗試從歐幾里得的五條公理開始，一步一步地從頭推論，於是原本只是三兩行的功夫，變成了兩大版的數學證明！事後數學老師當然有責備我，但是最後在那條題目也給了我滿分[2]。這就是數學只講邏輯的最好證明 — 只要邏輯正確，條條大路通羅馬。

2B Would you mind telling us a little bit about your research?
可以介紹一下您的研究嗎？

Prof. Julie Semmelhack : I work on the zebrafish visual system. We want to understand how the visual system works, how images get from the eyes to the brain, using zebrafish as a model. Historically people have used non-human primates, or even cats, but recently that has fallen out of favor partly due to ethical concerns, and partly because it is so difficult to map connections in primate brains, which has a larger number of visual areas.

We can use genetic tools on zebrafish; many labs around the world are working on building different strains of zebrafish that we use in research. They're also transparent at a young age (the larval stage), so we can use imaging techniques to see which neurons are active without having to do surgery. Zebrafish are vertebrates, so they are much more similar to human beings than insects. They are also highly visual animals, as they rely on visual cues to hunt animals and avoid predators.

Julie Semmelhack教授：我是研究斑馬魚視覺系統的；我的團隊希望明白視覺系統是怎樣運作的，影像如何從眼睛傳送到大腦，而我們的研究以斑馬魚作為模型。從前，科學家會用人類以外的靈長類動物，甚至貓作為模型，可是現在因為道德理由而棄用；另外亦是因為靈長類動物的大腦有很多個視覺區，我們很難整理當中錯綜複雜的關聯。

我們可以在斑馬魚上應用各種基因工具；世界各地實驗室也在繁殖不同品系的斑馬魚供研究使用。當斑馬魚還是幼魚的時候身體是透明的，因此我們可以透過成像技術看到神經元的活動而不用開刀。斑馬魚也是脊椎動物，因此和昆蟲相比，牠們與人類較為相似。另外斑馬魚是十分依賴視覺的動物，牠們靠著眼前的影像變化來獵食和避開捕食者。

3 What made you fall in love with science?
有什麼原因令您愛上科學？

Prof. Ivan Ip : I liked numbers and puzzles as a child. I also liked, and was quite good at, mental arithmetic – I could multiply 4-digit numbers in my head. But I was slow at reading so I wasn't interested in literature. I won't say I'm a particularly good leader, so I definitely wasn't a business person either. Therefore, it was really through an elimination process, I decided to pursue science from quite a young age.

In secondary school I joined the International Mathematical Olympiad – I trained for several years there, and they teach you the sort of math you'll never learn in high school, like writing proofs. So there I learned a lot of mathematical theories that might not be taught even at university, and that made me want to focus on math in the future.

I also liked reading encyclopedias when I was younger, so I was quite interested in space and all that. Later on I did study physics at university (here at HKUST). But I suppose my love for science really depended on my interest, and probably support from my family – my mother still complains about having to read aloud children's encyclopedias to me when I was young!

葉智皓教授：小時候我喜歡數字和拼圖，也喜歡而且頗擅長心算 — 我可以把四位數在腦內相乘。但是我閱讀的速度比較慢，所以對文學沒什麼興趣。我不會說我是一個特別好的領袖，所以也絕對不是一個生意人。因此，那正是在排除法之下，我年紀頗小就選擇了科學這條路。

在中學的時候我參加了國際數學奧林匹克，在那裡的幾年訓練教了我不少學校不會學到的數學，譬如證明的手法等等。我在那裡學到很多數學理論，它們甚至是大學也不會教的，而令我決定未來也要專注於數學。

稍為年幼的時候我也喜歡看百科全書，所以對太空之類亦頗感興趣。長大後我也有在大學修讀物理（就是在科大）。我認為我對科學的熱愛是興趣使然的，大概還有家人的支持吧 — 媽媽還在抱怨小時候要給我朗讀兒童百科全書呢！

Prof. Julie Semmelhack : I decided I wanted to become a scientist when I was in high school – around 16 or so, so fairly late in high school. Before that I wanted to be a writer. I really enjoyed my high school biology class, and I just liked the fact that you could explain things that existed in the natural world. That was when I wanted to do something in biology.

Julie Semmelhack教授：我在高中的時候，大約16歲左右才決定要成為科學家 — 所以是頗晚才決定的；在那之前，我想成為一個作家。我十分喜愛高中的生物課，喜歡的原因在於你可以對自然世界裡的事情作出解釋，正是那時令我萌生要在生物學上作出貢獻的念頭。

Visit our website at *sciencefocus.ust.hk* to read the complete interview with the two scientists!
請瀏覽《科言》網站 *sciencefocus.ust.hk*，閱讀兩位科學家的完整專訪！

4 Could you offer some advice to secondary school students who are interested in pursuing higher education in science?
您能對有志在大學修讀科學的中學生給一些意見嗎？

Prof. Ivan Ip : Science is a very wide field, so the most important thing is to read more and to be exposed to different topics. There are many things you can learn, but it's important to find what you're interested in. Even with subjects that you like, you might not understand everything at first when you read about it – and that's okay. The important thing is the exposure; when you've gone further and need that concept again, you can recall seeing it before, and then go back to revisit it.

In this digital world, YouTube is a great resource for popular science – from math to physics, to chemistry and life science. Bigger channels might be more credible sources of information, but you still have to judge whether the information is correct – for very well-known topics, the chance of mistakes going undiscovered is quite unlikely, and you can always refer to Wikipedia, which is quite reliable. But when you're talking about new results, like the Nobel Prize and recent science news, you really have to look at how accurate the reporting is. Avoid content farms, and not take everything in without thinking about it.

Last but not least, it's a good idea to join science summer camps and activities – I joined them for a few years myself, when I was in school. It's not just for the exposure to new knowledge, but you also get to know new friends who share the same passion for science as you do, which can be quite beneficial later on.

葉智皓教授：科學是一個非常廣闊的範疇，所以最重要的是多閱讀，並多接觸不同題材。可以學習的東西有很多，但重要的是找出自己對什麼感興趣。即使是自己喜愛的科目，你也未必能第一次就看懂全部內容 — 那絕對沒問題！最重要的是你曾經接觸過這些課題，如果你往後需要用到它的話，你會記得自己曾經看過類似的東西，然後可以再回到那裡嘗試重新理解它。

在這個數碼世界，YouTube是一個很好的科普資源：無論數學、物理，到化學和生命科學都包羅萬有。追隨者多的頻道或許是比較可靠的資訊來源，可是你仍需要自行判斷到底資訊是否正確。如果是眾所周知的課題，它們出錯而沒有人指證的機會頗低；你也可以參考維基百科，那亦是挺可信的。但是說到前衛的科學研究，像是諾貝爾獎或是最新的科學資訊的話，就一定要加倍注意報導的準確性，避開內容農場，不能不加思索就相信你讀到的一切。

最後，你可以參加不同的科學夏令營和活動。我在學生時期也參加過數個這類型的活動。這不單是為了學習新的知識，也是認識在科學上志同道合朋友的好機會，對日後可能也有益處。

Prof. Julie Semmelhack : I would say find the thing that motivates you, something that you're excited about, and it'll be relatively easy for you to do the hard work and learn the things that you need along the way. Science is something that explains the things in the natural world, so there's the freedom to ask whatever questions you want to ask.

Also, don't worry if you're not the best at math or computer science! It's good to know how to code these days if you're going into any science field, but you don't have to be the best at it. You just have to be able to do some of it and understand the concepts, and collaborate with people who know what to do!

Julie Semmelhack教授：我的建議是找一樣能令你有動力去做的事情，一個令你振奮的課題，那麼之後一路的艱苦工作和學習就會變得相對容易。科學是一門能夠解釋自然世界的科目，因此你可以隨意問你想問的所有問題。

另外，如果你不是數學或電腦編程的頂尖高手也不用怕！現在對於進入任何一個科學範疇，學會電腦編程當然最好不過，但是你不用成為編程的第一名。你只要學會部分的東西和明白背後的概念，然後和懂得編程的人合作就行了！

[1] **Euclid's axioms are the following:**

1. A straight line may be drawn between any two points.
2. Any terminated straight line may be extended indefinitely.
3. A circle may be drawn with any given point as center and any given radius.
4. All right angles equal one another.
5. If a straight line falling on two straight lines makes the interior angles on the same side less than two right angles, the two straight lines, if produced indefinitely, meet on that side on which are the angles less than the two right angles.

歐幾里得的五大公理如下：

1. 在任何兩點之間可以畫一條直線。
2. 任意線段能無限延伸。
3. 可以以任意點作圓心和任意距離作半徑畫出一個圓形。
4. 所有直角都相等。
5. 若兩條直線都與第三條直線相交，並且其中一邊的內角和小於兩個直角，則若這兩條直線無限延長，它們必定會在這邊相交。

The full text of Euclid can be found online: one of them, for example, is
《幾何原本》全文可在網上查閱，其中一個網站為：
https://mathcs.clarku.edu/~djoyce/java/elements/toc.html

[2] Prof. Ip remarked that his teacher was really nice, and you are not suggested to try this at school!
葉教授補充說他的老師確實很大方，我們並不建議你在學校裡嘗試！

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