SCIENCE FOCUS 科言

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Acknowledgements 特別致謝

Message from the Editor-in-Chief 主編的話

Dear Readers,

At the HKUST, in-person teaching has been fully resumed since September. The excitement from students who come to lecture theaters and laboratories is overwhelming! We also look forward to spreading the joy of science with you in upcoming outreach activities on campus.

In this issue, we continue to bring you stories on how scientific breakthroughs illuminate the past and prepare us for the future. During evolution, body functions can be gained or lost to ensure the survival of a species. Have you ever wondered why pre-historic penguins gave up on flying? Thanks to advanced DNA sequencing technologies, we have also learned a lot more about our extinct, distant relatives who once lived side-by-side with our ancestors. Fast-forward to the early 1900s, we take a look at experiments that led to the formulation of the periodic table. We also consider the science behind the blue sky, the preparation of hot chocolate and the nuisance of acne. Finally, we delve into the mathematical basis of data encryption and the method that can be used to separate different cell types in laboratories and clinics.

We have an exciting series of posts lined up for Instagram. Do join us there for "quick bites" of scientific intrigues of everyday life! Please leave comments and we will try our best to address your questions.

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

親愛的讀者：

科大從九月起已經全面恢復面授課程，學生們都帶著興奮的心情回到講堂和實驗室上課！我們亦希望把這份對科學的喜悅透過即將在科大校園內舉行的外展活動分享給您。

今期我們會繼續向您介紹一些照亮昨天和締造未來的科學突破。在進化過程中，物種可以透過獲得或失去身體功能使其得以延續，您有想過史前企鵝為什麼放棄飛行嗎？多虧DNA定序技術，我們現在也能認識更多關於我們的史前近親，這些已絕種的人類曾經與我們祖先在同一段時間生活在同一天空下。然後讓我們把時間快轉至1900年代，看看那些決定現代元素表排列方式的實驗。我們亦會從科學角度探討藍天的原理、沖調熱巧克力的小現象和暗瘡帶來的困擾。最後，我們更會討論數據加密的數學原理，以及在實驗室和診所內把不同種類細胞分開的方法。

一系列精彩有趣的網上內容已經準備好，記緊留意我們的Instagram以獲取關於日常生活的科學小知識！歡迎大家留言，我們會盡力解答您的問題。

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What's Happening in Hong Kong? 香港科技活動

Fun in Fall Science Activities 秋日科學好節目

Any plans for this Fall? Check out these science activities!

計劃好這個秋天的好去處了嗎？不妨考慮以下活動！

Secrets of the Universe 3D 穹蒼解密3D

The quest for understanding the origin of our universe has never ceased. Since the postulation of atom as the indivisible building block of matter by the Greek philosopher, Democritus, it was proven that atom can be further divided into subatomic particles like electrons, protons, and some even smaller elementary particles. Investigations into these particles may offer a glimpse of what had happened in the early universe.

This 3D dome show will introduce to you some powerful modern research facilities, such as the Large Hadron Collider (LHC) and the Laser Interferometer Gravitational-Wave Observatory (LIGO). The show details past discoveries and ideas that inspired the current generation of scientists. Don't miss it if you have unanswered questions about the universe!

Show period: July 1, 2021 – March 31, 2022

Time: 2:00 PM and 6:30 PM on Monday, Wednesday, Thursday and Friday (except public holiday)
12:30 PM and 5:00 PM on Saturday, Sunday and public holiday

Venue: Space Theatre, Hong Kong Space Museum

Admission fee: Standard admission: $32 (stalls), $24 (front stalls)
Concession admission: $16 (stalls), $12 (front stalls)

Remarks: Please refer to the museum's website for more details.

人類對宇宙起源的探求從不止息。自古希臘哲學家德謨克利特猜想原子是物質不可分割的基本單位後，科學家證實原子可以被分割成次原子粒子（例如電子和質子），甚至是更細小的基本粒子。研究這些粒子可能有助我們窺探宇宙初期發生的事情。

這個立體球幕電影會向您介紹一些強大的現代研究設備，例如大型強子對撞機（LHC）和激光干涉儀重力波觀測站（LIGO），亦會提供歷史脈絡讓您了解現今科學家是如何受過往發現和想法啟發。對宇宙起源抱有疑問的您請不要錯過！

展期：2021年7月1日至2022年3月31日

時間：星期一、三、四及五（公眾假期除外）
下午二時正及六時三十分
星期六、日及公眾假期下午十二時三十分及五時正

地點：香港太空館天象廳

入場費：標準票：32元（後座）；24元（前座）
優惠票：16元（後座）；12元（前座）

備註：更多詳情請參閱太空館網頁。

The Shaw Prize 2021 Exhibition 2021邵逸夫獎展覽

Established in 2002, the Shaw Prize recognizes currently active scientists with recent significant breakthrough in scientific work. It consists of three annual prizes: Mathematical Sciences, Life Science and Medicine, and Astronomy. In the exhibition, you can learn more about the 2021 Shaw Laureates and their scientific research.

Date: October 29, 2021 – January 5, 2022

Venue: 1/F Main Lobby, Hong Kong Science Museum

邵逸夫獎於2002年設立，設有三個獎項：數學科學獎、生命科學與醫學獎和天文學獎，頒發給現時活躍於研究工作並在近期取得突破性成果的科學家。透過今次展覽，您可以更深入認識今年的得獎者以及他們的科研工作。

展期：2021年10月29日至2022年1月5日

地點：香港科學館一樓大堂

From the Sky to the Sea:

The Evolution of Penguins

從翺翔天際到潛行深海：企鵝的進化

By Kit Kan 簡迎曦

When we think of birds, we often picture creatures that fly freely in the sky with their big strong wings. Some scientists believe that the last common ancestor of all living birds could fly [1], but many species have lost this ability during the course of evolution. Penguins, emus, ostriches and some species of ducks have all lost this ability. It is not difficult to imagine the benefits brought by flight. Being able to travel long distances and escape from predators make flying a valuable skill. So why did these birds lose their ability to fly? What have they gained from not flying? Why do they still have wings? We will answer all these questions using penguin as an example.

One simple explanation of why penguins gave up flying is the high energy cost of flight. A study on the two living birds that could both fly and dive showed that it is difficult to optimize wings for both flying and diving [2]. For wing-propelled diving, birds need a large body size and short flat wings with dense bones. However, for flying, they need a smaller body with larger wings to lift themselves off the ground. Since these features are exact opposites of each other, if a bird is to use its wings to propel through water to find food, it is unlikely that their wings are also optimized for flying, leading to a high energy cost.

Another dimension to the flightlessness of penguins has to do with ecology. According to genetic analyses, penguins' closest living relatives are the Procellariiformes, an order of birds that can all fly (footnote 1). The divergence of these two groups of birds are thought to have happened around 66 million years ago, at the end of the Cretaceous period [3], when an asteroid wiped out three-quarters of plant and animal species on Earth, including many marine predators [4, 5], opening the ecological niches in the ocean. In the absence of large marine animals, escaping from marine predators became less of a problem for the ancestors of penguins. Without the competition for food in the sea, travelling long distance for food was also unnecessary. Suddenly diving, which uses less energy and provides more food, became more desirable than flying.

Once penguin ancestors started underwater life, they quickly evolved and spread around the Southern Hemisphere. Penguin ancestors adapted to underwater life by evolving denser bones and shorter wings for diving, feathers that are impenetrable to wind and water and dark back and white front to camouflage them when viewed from both below and above when swimming in the sea [6]. In addition, since they no longer had to fly, and had better access to food, they used all the extra energy on growing larger. The largest living penguin is the emperor penguin, which grows up to 1.1-meter tall and weighs up to 40 kilograms [7], compared to the one kilogram in wing-propelled diving birds that can fly [2]. However, the size of living penguins hardly compares to some of their extinct relatives. Fossil records showed that a genus of extinct penguins, *Palaeeudyptes*, stood above two meters and weighed up to 115 kilograms [8], and *Anthropornis*, another extinct giant penguin was about 1.8-meter tall [9].

However, these giant penguins went extinct as other large marine animals, such as toothed whales and seals arose [10]. While there is no direct fossil record suggesting that large penguins competed with these large marine animals for food, it is likely that the rise and fall of large penguins are closely linked to the ecosystem in the sea.

Through millions years of evolution, penguins have become flightless seabirds with wings that are specialized for diving. Repurposing wings is not exclusive to penguins. Ostriches use their wings for balance and changing directions while running [11]. Emus stretch their wings to cool themselves down under hot weather [12].

Evolution is not just about acquiring new body features and behaviors, but to optimize the body to fit a certain environment. Sometimes, the loss of an ability may bring more benefits than harm.

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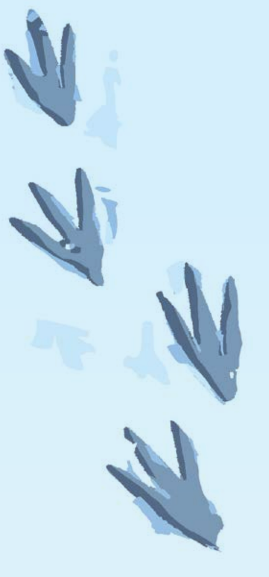
1 A prominent example of Procellariiformes is albatrosses (family Diomedeidae).



當提到鳥類時，我們經常會聯想到那些帶著強而有力的翅膀遨遊天際的生物。一些科學家認為所有現存鳥類的最後共同祖先都可以飛行 [1]，但許多鳥類物種在進化過程中已經失去了這種能力。企鵝、鴯鶓、鴕鳥和某些種類的鴨子都失去了飛行能力。飛行帶來的好處人所共知 — 能作長距離移動和逃離捕食者使飛行成為一項寶貴的技能。那為什麼這些鳥類在進化中失去飛行能力呢？牠們從不飛行中得到了什麼呢？為什麼牠們還有翅膀呢？我們將以企鵝為例回答這些問題。

企鵝放棄飛行的一個簡單原因是飛行的高能量成本。曾有研究分析過現存兩種既能飛行又能潛水的鳥類，發現翅膀很難同時迎合飛行和潛水 [2]。對於以翼推進的潛水，鳥類需要較大的體型和短而扁平、骨骼密度高的翅膀。然而，對於飛行，牠們需要較小的身體和較大的翅膀才能飛離地面。由於這些特徵彼此相反，如果一隻鳥透過用翅膀在水中推進以尋找食物，牠的翅膀並不太可能同時適合飛行，因為這會導致高昂的能量成本。

企鵝不會飛的另一方面與生態有關。根據基因分析，企鵝現存最密切的近親是鸌形目(Procellariiformes)的鳥類，當中所有成員都懂得飛行（註一）。這兩組鳥類的分化被認為發生在大約 6600 萬年前的白堊紀末期 [3]，當時一顆小行星毀滅了地球上四分之三的動植物物種，包括許多海洋捕食者 [4, 5]，打開了海洋裡的生態位。在沒有大型海洋動物的情況下，企鵝的祖先不再需要避開海洋裡的捕食者，加上不用與其他物種爭奪海洋裡的食物，也就再沒有必要長途跋涉去覓食。突然間，潛水變得比飛行更符合成本效益，它消耗更少能量並能提供更多食物。

企鵝祖先開始水中生活後，牠們迅速進化並散佈到南半球各地。企鵝的祖先進化出不同特徵來適應水中生活，包括密度更高的骨骼和更短的翅膀方便潛水，還有能夠擋風和防水的羽毛，以及黑色的背面和白色的正面令牠們在海中游泳時，從下方和上方觀察都有完美的保護色 [6]。此外，由於牠們不再需要飛行，並且可以更便利地獲得食物，牠們將所有額外能量用於增大體形。現存最大的企鵝是帝王企鵝，身高達 1.1 米，體重達 40 公斤 [7]；相比之下，同時可以飛行和以翼推進來潛水的鳥類體重只有一公斤 [2]。儘管如此，現存企鵝的體型與一些已滅絕的近親相比的話仍然相形見絀。化石記錄顯示，已滅絕的古冠企鵝屬（Palaeeudyptes）中的成員身高可達 2 米以上，體重則達 115 公斤 [8]，而另一種已滅絕的巨型企鵝 — 劍喙企鵝屬（Anthropornis）的成員則高約 1.8 米 [9]。

可是，這些巨型企鵝隨著其他大型海洋動物（如齒鯨和海豹）的出現而滅絕 [10]。雖然沒有直接化石記錄證明大型企鵝曾與這些大型海洋動物爭奪食物，但巨型企鵝的興衰很可能與海洋生態系統密切相關。

經過數千萬年的進化，企鵝變成了不會飛的海鳥，但卻擁有一雙為潛水而設的翅膀。改變翅膀用途的故事並不只是發生在企鵝身上：鴕鳥用牠們的翅膀在奔跑時保持平衡和改變方向 [11]，鴯鶓則在炎熱的天氣下張開翅膀降溫 [12]。

進化並不一定會帶來新的身體特徵和行為，反而是使身體適應特定環境。有時，喪失一種能力所帶來的好處可能多於傷害。

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1 鸌形目中的一個知名例子是信天翁（信天翁科）。

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The Mystery of the

By Henry Lau 劉以軒

What color is the sky? Most people, without thinking about it, would answer blue. That is indeed the correct answer, but why is that? Why can't it be green or yellow instead? The answer is more complex than you might think.

When discussing colors, we must always refer back to lights of different wavelengths. A specific wavelength gives a specific color that can be perceived by human eyes; for example, light with a wavelength of 450 nm gives a blue color while light with a wavelength of 650 nm gives a red color. What about sunlight? Sunlight appears to be white as it contains light of all wavelengths [1].

Light rays travel from the sun to Earth in a straight line. However, they can be intercepted, forced to abandon their initial trajectory and spread over all directions [2]. This phenomenon is known as Rayleigh scattering. Rayleigh scattering occurs when sunlight hits air molecules in the Earth's atmosphere. This causes the charged protons and electrons in the air molecules to oscillate, from which electromagnetic radiation at the same frequency is emitted to all directions [2]. Blue light, having short wavelengths and high frequencies, is scattered much more strongly than any other light that has a longer wavelength; in fact, the intensity of the scattered light was found to be proportional to the fourth power of the frequency [1, 2]. When we look at the sky, we are seeing the scattered light, and therefore the sky should look bluish-purple. However, our eyes are less sensitive to violet light [1, 2], and therefore the sky appears blue throughout the day.

Hang on, during sunset, the sky appears red. Why is that the opposite of what was described? That's because too much scattering of blue light has occurred. When the sun sets, it appears on the horizon. As we are probably looking directly at the sky in the vicinity of the sun on these occasions, it becomes the light rays which directly reach us that matter. During sunset (or sunrise), sunlight will have to travel a longer distance in the atmosphere than it had compared to when the sun was directly overhead at noon. This means blue light is scattered even more in the atmosphere, with the majority of it deflected to the directions away from us [3]. What can reach our eyes eventually becomes mostly the less scattered light with longer wavelengths. Since the light at those wavelengths appear red to us, the sky around the setting sun results in the familiar color of sunset red.

Another interesting fact is that the color of the sky is different depending on which planet you're on. It turns out that if you're on Mars, the sky appears reddish during the day and blue around the setting sun [4, 5], a complete inverse of what we're used to on Earth. This is because Mars' atmosphere is usually filled with dust, resulting in a different pattern of light scattering [4, 5].

Next time you go out on a summer's day, take a moment to appreciate our blue sky as well as the science behind its coloring. As long as we seek it, there will always be beauty in nature.

天空是什麼顏色？大多數人會不假思索地回答「藍色」。這是正確的答案，但為什麼是這樣呢？為什麼不能是綠色或黃色呢？答案可能比您想像的還要複雜得多。

說到顏色，我們不得不提及不同波長的光。不同波長分別對應著人眼可感知的不同顏色，例如波長為 450nm 的

Blue Sky 藍天之謎

光會呈現藍色，而波長 650 nm 的光會呈現紅色。那麼陽光呢？陽光看起來是白色，因為它包含所有波長的光 [1]。

光線從太陽沿直線照射到地球。可是，它們有可能被阻截，而被迫放棄原來軌跡並向各個方向散射 [2]，這種現象被稱為瑞利散射（Rayleigh scattering）。它發生在陽光擊中地球大氣中空氣分子的時候，這導致空氣分子中帶電的質子和電子產生振盪，因而向各個方向發射相同頻率的電磁輻射 [2]。藍光的波長很短、頻率很高，比其他具有更長波長的光線散射得更強烈。事實上，散射光的強度，是與其頻率的四次方成正比的 [1, 2]。當我們抬頭望向天空時，我們看到的是散射光，因此天空看起來應該是藍紫色的。然而，我們的眼睛對紫光敏感度較低 [1, 2]，所以天空在日間看起來是一片藍。

等等 — 日落時分，天空呈橙紅色。為什麼這與上述的情景是相反的呢？這是因為藍光過份散射所致。當太陽落山時，它位於地平線附近。由於我們觀看日落時都是望著太陽附近的天空，因此變了直接照射我們的光線才是決定天空顏色的。與中午當頭的烈日相比，在日落（或日出）時，陽光必須在大氣中穿過更長的距離，意味著藍光在大氣中的散射會更多，大部分藍光會散射到偏離我們的方向 [3]。因此， 最終可以到達我們眼睛的大多都變成了波長較長、散射較少的光。由於這些波長的光對我們來說是紅色的，落日周圍的天空因此染著我們熟悉的夕陽紅。

另一個有趣的事實是，天空的顏色會因應您所在星球的不同而改變。事實證明，如果您身處火星，白天的天空看起來是偏紅的，而落日周圍則是藍色的 [4, 5]，這與我們在地球上的認知完全相反。原因是火星的大氣層通常充滿塵埃，導致光線有著不同的散射模式 [4, 5]。

下次您在夏日外出時，不妨花點時間欣賞我們的藍天以及其背後的科學。只要我們肯去尋找，就可以看到大自然美麗璀璨的面貌。

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Physics in Yo

熱巧克力裡的物理

If you are someone who loves coffee, like me, then you will love it even more when you learn that there is a fun and delicious experiment you can do with your cup of coffee called the Hot Chocolate Effect. All you need for this experiment is a cup, hot water, a metal spoon, and instant coffee or cocoa powder – all of which can be obtained from your own kitchen. And the best part about this experiment is that you can enjoy a great cup of coffee afterwards.

The Experiment

- Unlike a regular cup of coffee, start by pouring hot water into the cup first, leaving a little room for the coffee powder to be added later.
- Lift your mug by holding the handle and tapping the bottom with a metal spoon. Listen to the knocking sound carefully and remember the tone.
- Pour the coffee powder into the cup and stir vigorously.
- Tap the bottom of the cup continuously while the liquid is swirling. Note that the starting note will be lower than the previous note but will increase with each tap until it is restored.
- Stir the liquid again and you can lower the pitch one more time and repeat the observation.
- Remember to enjoy your cup of coffee while it is warm!

The Explanation

What is the possible explanation behind this simple phenomenon? The answer lies behind the propagation of sound in a liquid and was explained in 1982 by Frank S. Crawford [1], an American physicist and a talented musician from University of California, Berkeley.

The phenomenon can be described using simple physics you might have learned from your science class. Consider the cup as a closed-end organ pipe. The frequency heard is the fundamental frequency, i.e. the lowest frequency and longest wavelength pattern the pipe can produce, in which the wavelength equals four times the height of your container. By substituting $\lambda = 4h$ into $v = \lambda f$, you will get:

$$f = \frac{v}{\lambda} = \frac{1}{4}\frac{v}{h}$$

Here f is the sound frequency, λ is the wavelength, v is the speed of sound, and h is the height of the cup. The height and shape of the cup does not change as you tap, so it must be the speed of sound in the liquid that is increasing!

Then why is the speed of sound increasing? It is because the bubbles trapped in the coffee powder are released into the liquid when you vigorously stirred the coffee. Sound travels faster in liquid than in the air. Therefore, the bubbles in liquid slow down the overall speed of sound, and lower the fundamental frequency. More precisely, the air bubbles reduce the bulk modulus (see text box) of the liquid by making it more compressible or springy. As time goes by, air bubbles in the liquid will escape gradually. Therefore, the speed of sound is slowly rising – along with the pitch of the sound produced!

> Bulk modulus is also known as the incompressibility of a material. It defines how resistant a material is to compression. For example, air is less resistant than liquid, so air has a lower bulk modulus. The speed of sound in a material is given by:
>
> $$v = \sqrt{\frac{K}{\rho}}$$
>
> where K is the bulk modulus and ρ is the material density. The change in material density is negligible in our experiment.

A very simple yet exciting and fun effect, isn't it? There are many other variations of this effect you can explore by yourself! For example, try substituting the powder with other soluble substances like powdered milk or baking soda. Try to adjust the water temperature or use a taller container. You may also try it with soft drinks and beer as well. The next time you are enjoying your favorite beverage, there might be another interesting physics phenomenon waiting to be discovered!

ur Cup of Hot Chocolate

By Randy Stefan Tanuwijaya

如果您像我一樣是咖啡愛好者的話，那麼，您知道以下一個關於熱巧克力效應（Hot Chocolate Effect）的簡單實驗後，一定會更喜愛咖啡。這個有趣又美味的實驗需要的材料垂手可得 — 就是您手上的那杯咖啡。更具體地說，我們需要一隻杯、熱水、一枝鐵匙和即溶咖啡粉或可可粉 — 這些都是在廚房可以找到的。這個實驗的吸引之處是完結時您可以享用到一杯醇厚的咖啡。

實驗步驟

- 與平時不同，先把熱水倒進杯裡，留少許空間給稍後加入的咖啡粉。
- 透過杯耳拿起杯子，用鐵匙輕敲杯底。細心聆聽敲擊聲，並記住音調。
- 把咖啡粉倒進杯裡，快速攪拌。
- 趁杯中液體還在旋轉時，連續敲擊杯底。第一下敲擊聲會比之前沒有咖啡粉的低音，但音調會隨每下敲擊提高，直至回復為止。
- 再次攪拌液體，音調會再一次降低。聆聽敲擊聲的改變。
- 記得在咖啡冷掉之前享用咖啡！

實驗解說

這個簡單現象背後的解釋會是什麼呢？答案關乎聲音在液體中的傳播。同時是天才音樂家的加州大學柏克萊分校美籍物理學家 Frank S. Crawford 曾在 1982 年對這個現象作出解釋 [1]。

解釋這個現象只需簡單物理，涉及的定理您可能也在課堂中學過。我們可以把杯子看成一端封閉的閉管樂器，然後我們聽到的頻率是基頻（fundamental frequency），那是閉管能夠產生而擁有最低頻率和最長波長的聲波，其波長等於我們容器高度的四倍。把 $\lambda = 4h$ 代入 $v = \lambda f$，我們可以得到：

$$f = \frac{v}{\lambda} = \frac{1}{4}\frac{v}{h}$$

這裡 f 是聲音頻率，λ 是波長，v 是聲音傳播的速度，h 是杯的高度。由於杯的高度和形狀都不會隨著我們敲擊而改變，那增加的一定是聲音在液體傳播的速度！

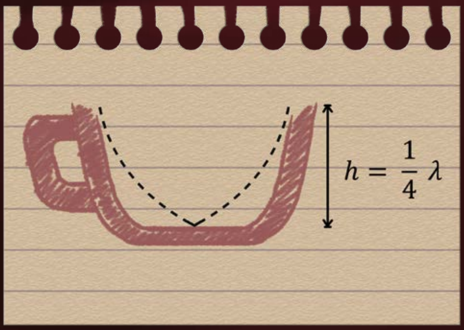
那麼，為何增加的是聲音傳播的速度呢？這是因為困在咖啡粉之間的氣泡會在您劇烈攪拌咖啡時被釋放出來。由於聲音在液體中傳播的速度比在空氣中快很多，因此氣泡會減慢聲音傳播的整體速度，基頻亦會被降低。更準確地說，氣泡降低了液體的體積彈性模量（bulk modulus；見註釋），令液體更具壓縮性（或彈性）。隨著氣泡逐漸從表面逃逸，聲音傳播的速度會慢慢回升，令音調亦隨之上升。

體積彈性模量又稱為物質的不可壓縮性，即是其抗壓縮的能力。譬如說，空氣的抗壓縮能力比液體低，空氣因此有較低的體積彈性模量。聲音在某物質中的傳播速度可以用以下公式表達：

$$v = \sqrt{\frac{K}{\rho}}$$

公式中的 K 是體積彈性模量，ρ 是物質的密度。在我們的實驗中，物質密度的改變是可忽略的。

這個小現象雖然簡單，但不是又好玩又有趣嗎？這效應也有著不同的版本，您不妨逐一嘗試！譬如您可以嘗試改用其他可溶物質，例如奶粉和蘇打粉，也可以改變水溫或用更高身的容器。另外，試試用汽水或啤酒也不錯。下次在享用您最愛的飲料時，可能也有另一個有趣的物理現象等著您發現。



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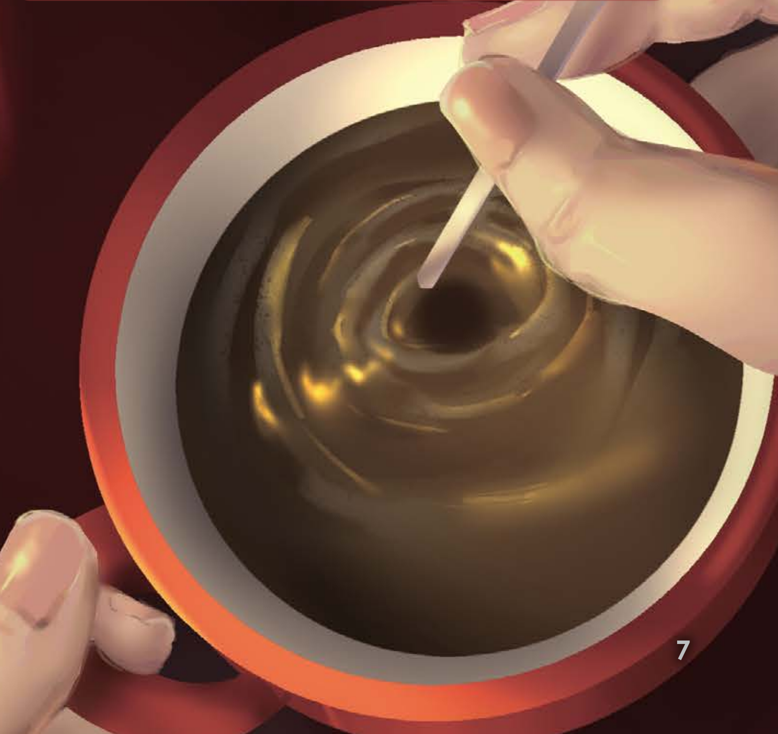


Genetic Inheritance From Our Long-Lost Relatives
從遠古近親而來的遺傳訊息

By Sirius Lee 李揚

Human From the Neander Valley

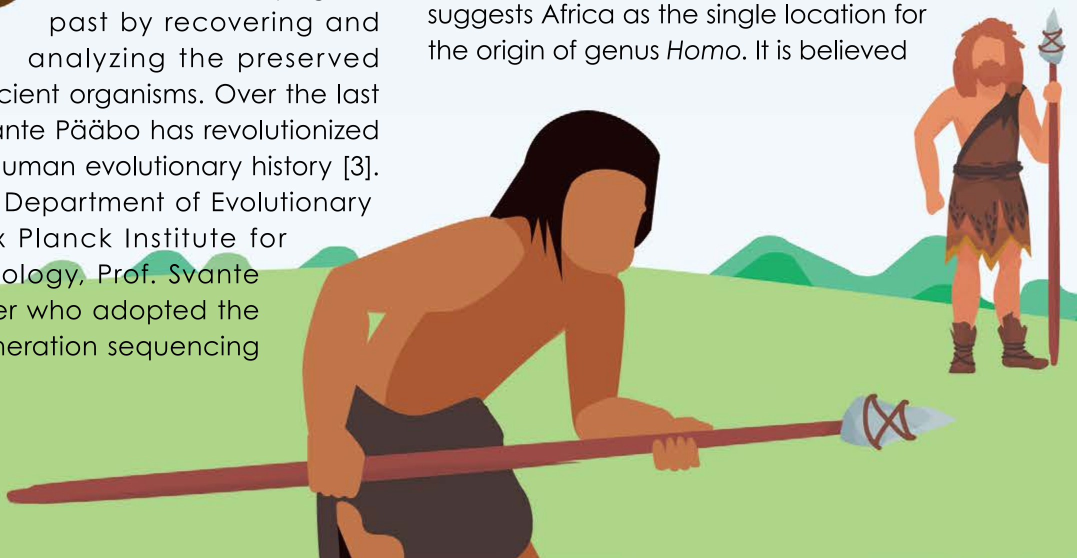
Sharply distinguished by our unique mode of cognition, we humans possess intellectual capacity that are incomparable to most living organisms, and were scientifically named *Homo sapiens*, which implies "wise man" in Latin. Yet, there was once a species who shared a surprisingly similar appearance with us, and managed to create tools for domestic uses such as sharpened spears to kill animals for food [1]. They are described as our sister species and our distant relative, whose major specimen was first discovered in 1856 in the Neander Valley in Germany. Anthropologists therefore name them *Homo neanderthalensis*, meaning "human from the Neander Valley" [2].

Spotlight on the Pioneer – Svante Pääbo

Paleogenetics is the field of studying the past by recovering and analyzing the preserved genetic material in ancient organisms. Over the last four decades, Prof. Svante Pääbo has revolutionized our understanding of human evolutionary history [3]. As the Director of the Department of Evolutionary Genetics at the Max Planck Institute for Evolutionary Anthropology, Prof. Svante Pääbo was the pioneer who adopted the cutting-edge next-generation sequencing technology in paleogenetics and contributed to overcome the technical obstacles encountered [4]. In 2002, his team published a paper on the evolution of the gene FOXP2, which sparked wide interest in its possible role on the ability of humans to articulate speech and develop language [5, 6]. In 2006, he initiated a project to sequence the entire Neanderthal genome; a draft sequence was eventually published in May 2010 [7]. In March 2010, he identified an extinct human species, Denisovan, which was previously unknown [8]. These contributions have profound influence on our understanding of human evolution and our ancient relatives.

Legacy From Neanderthals in Our DNA

With the three billion-letter Neanderthal genome first sequenced in 2010, it was revealed that Neanderthal DNA is approximately 99.7% identical to modern human DNA [6]. Close phylogenetic relationships between *Homo sapiens* and *Homo neanderthalensis*, where the two species shared a common ancestor 400,000 to 700,000 years ago, can be concluded by genomic calculations and fossil record [9-11]. Most striking of all, by looking into the genomes of five present-day humans from different continents, 2% of the non-African modern human genome was proven inherited from Neanderthals, whereas no Neanderthal DNA could be found in the genomes of the two Africans [9]. Despite of the limited sample size, the result seems to support the famous "out-of-Africa" model, a hypothesis which suggests Africa as the single location for the origin of genus *Homo*. It is believed



that the genus *Homo* migrated out of Africa in a few waves [12]. Modern humans were speculated to have encountered and interbred with the Neanderthals and Denisovans who had left Africa much earlier, when we first spread out of sub-Saharan Africa [12]. The interbreeding hypothesis is now supported by the results of many genetic analyses [13, 14], including the 2% inheritance of Neanderthal DNA exclusively found in non-African genomes in the study above [9].

Not only did we find evidence that reconstructed our genealogy, we also found traits linked to these remnants in our DNA. Published in *Nature* in September 2020, a genomic segment inherited from Neanderthals on the third chromosome has been identified as a risk locus for respiratory failure after infection of SARS-CoV-2 [15], meaning that the genomic location may contain a version of gene (scientifically termed an allele) associated with an increased risk of severe infection and hospitalization. That allele concerns around 50% and 16% of south Asia and European populations respectively [15]. Scientists posited that the allele could once confer a significant survival advantage on individuals by its ability to elicit a protective immune response against ancient pathogens, so that it was positively selected for in some populations during the course of natural selection [16]. However, the ancient genes may be unfavorable today as the immune response induced could be overly aggressive and potentially fatal in a COVID-19 infection [15].

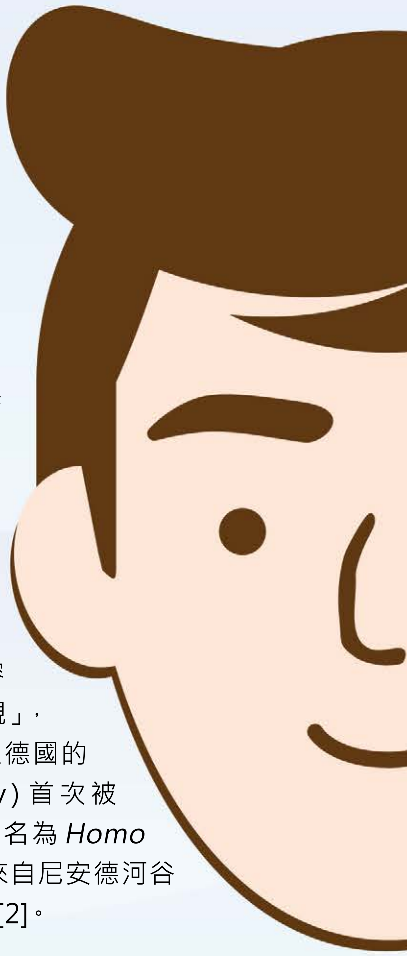
Our Second Distant Relative – Denisovans

The tree of evolution is continuously being tangled with additional discoveries of human ancestry. Besides the archaic humans Neanderthals, Denisovans lived about 40,000 to 400,000 years ago in Europe and Western Asia [17]. This group of extinct human species was first identified by Prof. Pääbo from the genetic material recovered from a finger bone fragment collected from Denisova Cave in the Altai Mountains of Russia, which gave rise to the name "Denisovans" [18]. Anatomically, Denisovans were speculated to have an elongated face, a wide pelvis, an increased dental arch and lateral cranial expansion [19].

Genetically, there was also evidence of interbreeding between Denisovans, Neanderthals and ancestors of modern humans [11, 20]. Traces of Denisovans can primarily be found nowadays in the genomes of Southeast Asian and Pacific Islander populations, whereas people in other parts of the world contain only a very low or an undetectable amount of Denisovan DNA sequence [17]. Similar to the genetic variations inherited from Neanderthals, genetic variants from Denisovans may also contribute to many of our traits, for example, hair texture, height, sensitivity of smell and immune responses [17].

The Quest to Answer the Unanswered

The rise of human ancient DNA research not only feeds our mere curiosity, but also provides us new insights on how the course of evolution shapes human into the creature we are today; or in other words, what makes humans human. The fascinating findings on human adaptation and disease susceptibility through time also reveal many intriguing facts about ourselves, not least, to be aware that there is so much we do not know. How many of you would like to follow the footsteps of Prof. Pääbo?



來自尼安德河谷的人類

有著與別不同的認知模式，我們人類擁有大多數生物皆無法比擬的智慧，在科學上被名為 *Homo sapiens*，拉丁語上解作「智人」。然而，過去曾有物種與我們有著意外地相似的外貌，他們也懂得運用自製工具，例如使用打磨過的鋒利長矛打獵 [1]。被形容為我們的「姊妹物種」或「遠親」，他們的主要遺骸於 1856 年在德國的尼安德河谷(Neander Valley)首次被發現，人類學家因此將他們命名為 *Homo neanderthalensis*，意思是「來自尼安德河谷的人類」[2]。

古遺傳學先鋒 — Svante Pääbo

古遺傳學是透過提取和分析殘留在古代生物中的遺傳物質來研究過去的一門學科。在最近四十年，Svante Pääbo 教授徹底改變了我們對人類進化歷

史的理解 [3]。Pääbo 教授以馬克斯•普朗克進化人類學研究所進化遺傳學系主任的身份，率先把尖端的次世代定序法應用在進化遺傳學上，並參與解決過程中遇到的技術障礙 [4]。2002年，他的團隊發表了關於 FOXP2 基因演化的論文，引發學術界對了解其在人類發展說話能力和語言上可能扮演角色的廣泛興趣 [5, 6]。2006年，他展開了找出整個尼安德特人（Neanderthal）基因組序列的研究項目，而序列草稿最終於 2010 年 5 月發布 [7]。2010 年 3 月，他又發現了另一個已滅絕人類物種 — 丹尼索瓦人（Denisovan） [8]。這些貢獻都對我們有深遠的影響，改變了我們對人類進化和遠古近親的認知。

尼安德特人在我們 DNA 中的遺痕

隨著長達三十億個字母的尼安德特人基因組在 2010 年被首次測序，它揭示了尼安德特人和現代人類 DNA 的相似度達 99.7% [6]。對基因組作出的計算和化石記錄推測，*Homo sapiens* 與 *Homo neanderthalensis* 在 400,000 至 700,000 年前擁有共同祖先，兩者之間有著密切的親緣關係 [9-11]。最引人注目的研究結果是，透過分析來自不同大陸五個現代人類的基因組，我們發現非非洲裔現代人類基因組中的 2% 是從尼安德特人遺傳下來的，而在兩個非洲人的基因組中並沒有發現尼安德特人的 DNA [9]。儘管樣本數量有限，但結果似乎支持著名的「源出非洲」模型，即是假設非洲是人屬（*Homo*）的單一起源地。研究人員相信人屬在歷史上曾分幾次遷離非洲 [12]，並猜測當現化人初次遷出撒哈拉以南非洲地域的時候，我們遇到了更早離開非洲的尼安德特人和丹尼索瓦人並與其雜交 [12]。雜交假說現在得到許多遺傳學分析的支持 [13, 14]，包括上述只在非非洲裔基因組中發現 2% 尼安德特人 DNA 的研究 [9]。

我們不僅找到更多證據來重整我們的系譜（genealogy），更找到與這些 DNA 印記相關的性狀（traits）。2020 年 9 月一篇發表在《自然》期刊的論文指出，人類第三對染色體中遺傳自尼安德特人的一個片段被確定是感染 SARS-CoV-2 後呼吸衰竭的風險位點（risk locus）[15]，意思是該處可能含有一個版本的基因（科學上稱為等位基因），它與嚴重感染和住院風險有關。該等位基因分別影響約 50% 和 16% 的南亞和歐洲人 [15]。科學家認為，該等位基因過往可能有助引發針對古代病原體的免疫反應，賦予個體顯著的生存優勢，因此在物競天擇的演化過程下被揀選而在一些族群中得以保留 [16]。可是，這些古老基因在今天卻可能對我們不利，因為在 COVID-19 感染中它們可以引起過份強烈，甚至是致命的免疫反應 [15]。

我們的第二個遠親 — 丹尼索瓦人

越來越多關於人類祖先的發現亦令進化樹的分枝繼續糾纏。 除了古代人類尼安德特人以外，丹尼索瓦人（Denisovans）也大約在 40,000 到 400,000 年前在歐洲和西亞居住 [17]。這群已滅絕的人類物種由 Pääbo 教授從手指骨碎片提取的遺傳物質中被初次發現，由於該樣本取自俄羅斯阿爾泰山脈丹尼索瓦洞穴（Denisova Cave），因此這群人類被稱為「丹尼索瓦人」[18]。在解剖學上推斷，丹尼索瓦人應該具有長形的臉、寬闊的盤骨、較長的牙弓和側向擴張的顱骨 [19]。

在基因上，也有證據顯示丹尼索瓦人、尼安德特人和現代人祖先之間曾經雜交過 [11, 20]。丹尼索瓦人的痕跡現在主要可以在東南亞和太平洋島民人口的基因組中找到，而世界其他地區的人則只含有非常低的，或是無法檢測到丹尼索瓦人 DNA 序列 [17]。與從尼安德特人得來的遺傳變異相似，來自丹尼索瓦人的遺傳變異也會參與塑造我們許多特徵，例如頭髮質地、身高、嗅覺敏感度和免疫反應 [17]。

探索未知的過去

人類古代 DNA 研究的興起不僅是滿足我們單純的好奇心，也為我們提供了一些新見解，解釋進化過程如何把我們塑造成今天的人類；換句話說，是什麼令人類擁有人類的特質。關於人類在適應環境和疾病抵抗性上改變的這些驚奇發現，揭示了許多關於我們人類自身的有趣事實，亦讓我們意識到我們所知的其實只是冰山一角 — 你們未來願意追隨 Pääbo 教授的步伐嗎？

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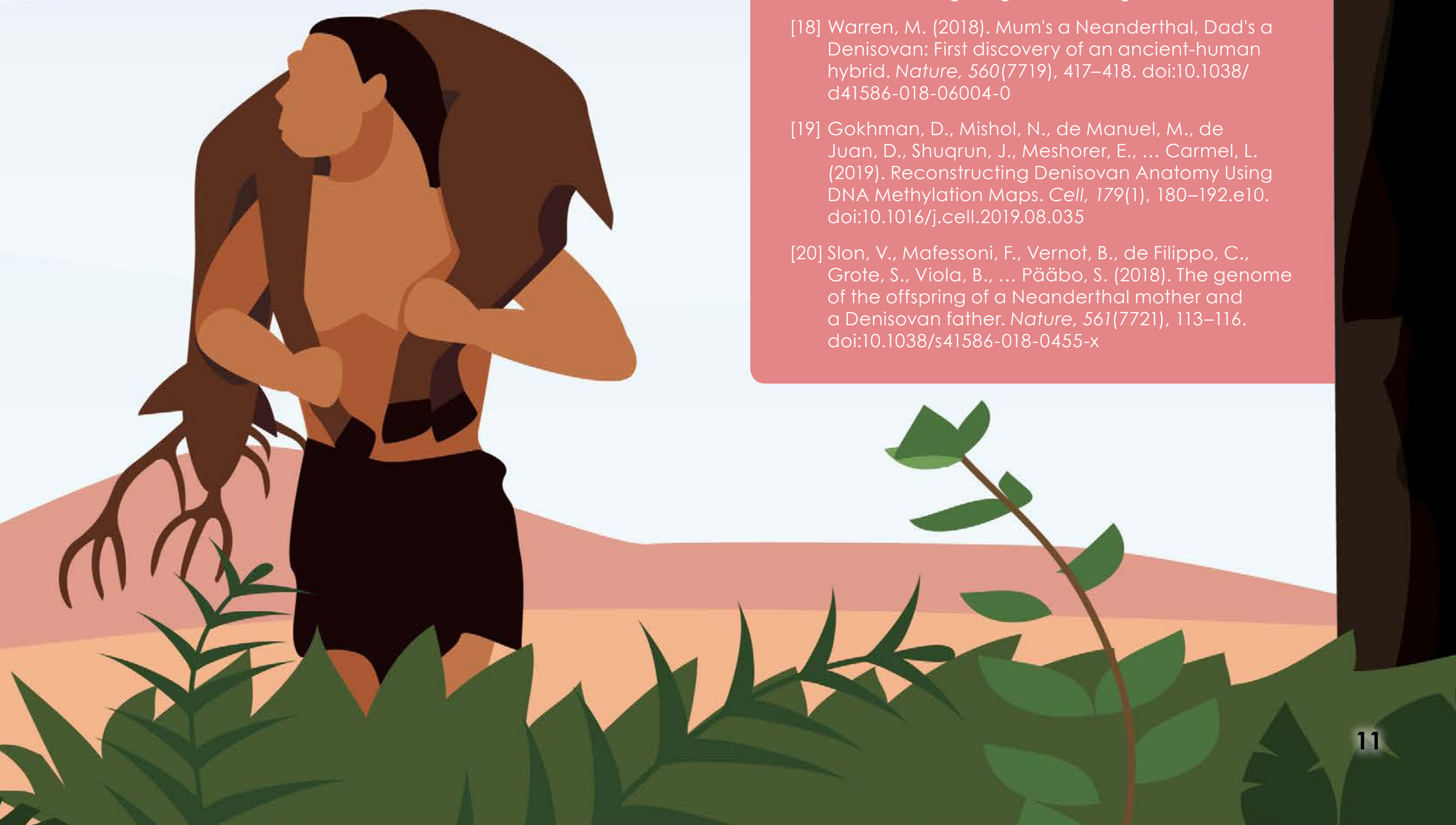

The Science of Acne

流言終結者：暗瘡篇

By Paolo Miguel Magallanes Mallorca

Have you ever woken up one day, looked in the mirror, and seen several new pimples on your face? If yes, then these pimples could be acne (or acne vulgaris).

Acne arises from inflammation occurring on the skin. To be exact, it occurs on the pilosebaceous units. These are skin pores responsible for hair growth and sebum production. Acne can be found most commonly on faces, forehead, neck, upper chest, and shoulders, where pilosebaceous units are abundant [1]. There are three common observations associated with acne formation: overproduction of sebum, infection by skin bacteria, and abnormal follicular keratinization [2].

Overproduction of Sebum

As mentioned earlier, the pores produce sebum. Sebum is an oily liquid that protects our skin from harmful bacteria and dryness. However, too much sebum can clog the pores, causing acne to form. The production of sebum is controlled by many different factors, but one of the well-studied factors is androgens [2, 3]. Androgens are sex hormones responsible for bodily changes during puberty. Since androgen levels increase dramatically during puberty, the hormone can also cause the overproduction of sebum [3, 4]. This is why acne outbreaks are common during teenage years.

Infection by Skin Bacteria

Certain species of bacteria live on our skin. One of them, known as *Cutibacterium acnes* (formerly *Propionibacterium acnes* [5]), may involve in acne formation. *C. acnes* feeds on sebum, and when there is excess sebum, the bacterial population can grow and multiply. The pores clogged with excess sebum can become infected with *C. acnes*, which may aggravate inflammation around the area and result in acne [2, 6].

By comparing the strains of *C. acnes* in the pilosebaceous units on the noses of acne patients and healthy individuals, researchers reported that certain strains were strongly associated with acne but some were linked to healthy skin [7]. Revealed by genomic analysis, each of these strains contains unique genetic elements that could potentially contribute to the formation of acne or maintain skin health [7]. Further investigation on the functions of these strains could help shed light on the pathogenesis of acne and may ultimately lead to the development of targeted therapeutics [7].

Abnormal Follicular Keratinization

Keratinization is the process where a type of skin cells, keratinocyte, hardens itself with keratin proteins [8]. The hardened cells are pushed towards skin surface to form a protective layer, such as stratum corneum, which provides protection against infection, desiccation and mechanical stress [8]. However, follicular hyperkeratinization is observed in acne patient, from which a thickened layer of stratum corneum forms due to the deposition of excess keratin [6, 9]. Such a keratinous plug blocks the follicle and provides an anaerobic environment for the proliferation of *C. acnes* [10, 11], while the bacteria is also known to influence keratinization by secreting propionic acid (IUPAC name: propanoic acid), leading to skin cells with altered shapes [2]. These altogether result in the formation of comedo.

Below are some common misconceptions people may have about acne.

Myth #1: Only teenagers get acne.

Fact: While it is true that the many cases of acne outbreaks occur during puberty, acne outbreaks can occur anytime beyond age 20. For instance, acne outbreaks can occur before menstruation or during pregnancy in females, probably due to hormonal changes [3, 4, 11]. Stress can also lead to acne through the elevated level of stress hormones [2]. However, the underlying cause of postadolescent acne is largely unknown [11].

Myth #2: Washing your face more often will cure acne.

Fact: While this seems logical, there is no strong evidence that washing more would cure acne [10]. Antibacterial skin cleansers and acidic cleansing bars might have marginal effect on mild acne [10]. However, excessive face washing may unnecessarily remove sebum on the skin surface that normally functions to retain moisture. It dries the skin and causes the compensatory overproduction of sebum, therefore defeating the purpose of the treatment [10].

Myth #3: Eating oily food will cause acne.

Fact: There is not enough scientific evidence yet to prove that dietary fat [13], or any single food [14], can cause acne. However, speaking of diet, previous studies indicated that reducing glycemic load on diet might improve the outcome of acne [10]. Acne also seemed to be correlated with obesity [2, 10], but no evidence has proven yet that dietary restriction reduces acne [10]. More study is needed to show the causation between diet and acne [2].

Myth #4: It is OK to pop your pimple.

Fact: It's not okay to pop your pimple on your own. Popping them with bare hands can bring more bacteria to the area and worsen the inflammation. Dermatologist are trained to do proper acne removal with sterile instruments if needed, although this is usually done only when other treatments don't work [15].

Generally, if your acne condition persists or worsens, it's advisable to seek advice from a dermatologist. A combination of topical retinoid and antimicrobial therapy can be prescribed to suppress inflammation by blocking the inflammatory pathways in our body and controlling the growth of *C. acnes* [16]. It can also reduce the blockage of pilosebaceous units by inhibiting the proliferation of keratinocytes [16].

你試過一覺醒來望向鏡子，然後發現臉上新長了幾顆痘痘嗎？有的話，那可能就是暗瘡了（英文叫「acne」或「acne vulgaris」）。

暗瘡由皮膚發炎所致，準確來說是發生在毛囊皮脂腺單位（pilosebaceous units）的炎性反應，這些毛孔負責長出毛髮和製造皮脂。暗瘡常見於毛囊皮脂腺單位豐富的位置，包括面部，還有額頭、頸、上胸和肩膀 [1]。暗瘡的形成通常涉及以下三個現象：皮脂分泌過盛、皮膚細菌感染和毛囊異常角質化 [2]。

皮脂分泌過盛

如前文所述，毛孔分泌皮脂，它是一種保護皮膚免受細菌傷害和防止皮膚乾燥的油性液體。可是，過多的皮脂會塞住毛孔，形成暗瘡。皮脂分泌受多個因素控制，其中一個經常被研究的是雄性激素 [2, 3]，它們是青春期引起身體變化的性激素。雄性激素水平會在青春期大幅提升，它們亦能導致皮脂過度分泌 [3, 4]，這正是為什麼暗瘡通常出現於青春期的原因。

皮膚細菌感染

有些細菌居住在我們皮膚表面，其中一種是 *Cutibacterium acnes*（舊稱 *Propionibacterium acnes* [5]），它們可能參與暗瘡的形成。*C. acnes* 以皮脂作為食物，當有多餘皮脂的時候細菌種群能生長和大量分裂。被多餘皮脂塞住的毛孔就可能被 *C. acnes* 感染，加劇周邊的炎性反應並引起暗瘡 [2, 6]。

透過比較暗瘡患者和健康人士鼻上毛囊皮脂腺單位中的 *C. acnes* 菌株，研究人員指出一些菌株與暗瘡有著密切關聯，亦有一些是與健康皮膚有關的 [7]。基因組分析揭示了這些菌株都有一些獨特的基因元件，它們可能對形成暗瘡或維持皮膚健康起作用 [7]。對這些菌株的功能作進一步研究可能有助闡明暗瘡的病理，最終有助發展出針對性的療法 [7]。

毛囊異常角質化

角質化是一種名為角質細胞的皮膚細胞硬化的過程，當中涉及角蛋白 [8]。這些硬化了的細胞會被推至皮膚表面形成保護層，例如角質層，保護皮膚免受感染、乾燥和物理應力影響 [8]。可是，在暗瘡患者上會觀察到毛囊過度角質化的現象，即是過多的角蛋白令角質層異常地加厚 [6, 9]，形成角質化塞子堵住毛囊，提供無氧環境令 *C. acnes* 滋生 [10, 11]。另一方面，*C. acnes* 亦會透過分泌丙酸影響角質化，令皮膚細胞有著異常的形狀 [2]。這些過程都會導致粉刺形成。

以下是一些人們對暗瘡的普遍誤解。

流言一：只有青少年會長暗瘡。

事實：暗瘡的確很多時都出現在青春期，但 20 歲後也可能隨時出現，例如暗瘡可以出現在女性月經前或懷孕時，這可能是由於荷爾蒙水平改變 [3, 4, 11]。壓力也可以令壓力荷爾蒙水平上升而引發暗瘡 [2]。可是，成年人長暗瘡的成因在很大程度上仍然有待發掘 [11]。

流言二：多洗臉可以治好暗瘡。

事實：雖然這聽起來好像合符邏輯，但並沒有具說服力的證據顯示多洗臉可以治好暗瘡 [10]。抗菌洗面乳和酸性潔面皂對輕微暗瘡可能有少許幫助 [10]。然而，過度洗臉可能不必要地清除正常功能是保持皮膚濕潤的皮脂，這反而會令皮膚變得乾燥，使其分泌更多皮脂以作補償，因此不能達到治療的目的 [10]。

流言三：吃油膩的食物會導致暗瘡。

事實：沒有足夠科學證據證明膳食脂肪 [13] 或者任何一種食物 [14] 足以引發暗瘡。可是說到膳食，過去研究指出減低膳食的升糖負荷（glycemic load）可能有助改善暗瘡情況 [10]。暗瘡亦似乎與肥胖有關 [2, 10]，但沒有證據顯示節食能減少暗瘡 [10]。膳食和暗瘡之間的因果關係尚待進一步研究探討 [2]。

流言四：擠暗瘡是 OK 的。

事實：自己擠暗瘡是不 OK 的。徒手擠暗瘡會為患處帶來更多細菌，加劇炎性反應。皮膚科醫生受過訓練，在有需要的情況下會用無菌工具移除暗瘡，儘管這通常是在其他方法都行不通時才會做 [15]。

一般來說，如果暗瘡情況持續或惡化的話最好去咨詢皮膚科醫生。醫生可能會採用外用 A 酸（topical retinoid）及抗微生物藥的混合療程，以堵截身體內導致炎性反應的生化途徑和抑制 *C. acnes* 的生長達到消炎效果 [16]，它也可以透過抑制角質細胞的分裂來減少對毛囊皮脂腺單位的阻塞 [16]。

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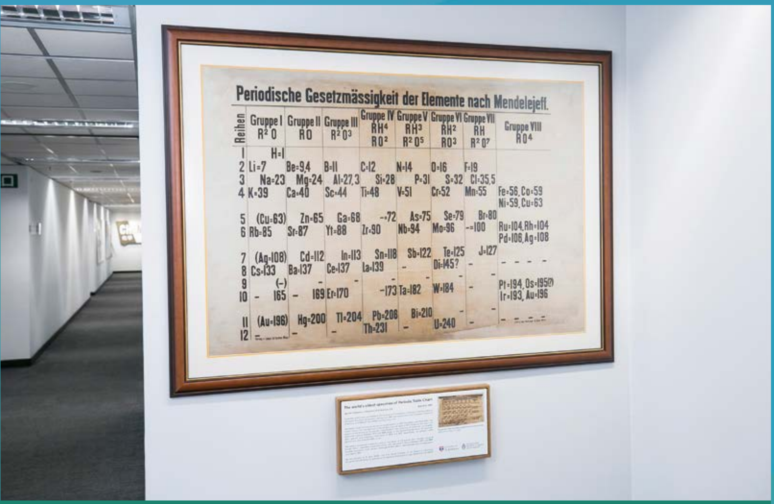
The Periodic Table Putting Each Element in the Right Spot

怎樣「證明」元素表的排列是對的？

By Peace Foo 胡適之

At the beginning of the 20th century, scientists still weren't sure what to make of the periodic table. Older classifications of the chemical elements ran in order of increasing atomic weight. Dmitri Mendeleev's table aimed to capture periodic trends in their properties, the so-called Periodic Law, forcing him to relegate atomic weights to a secondary consideration [1]. For example, cobalt has a greater atomic weight than nickel, yet the Periodic Law dictates that cobalt comes before nickel based on its chemical properties. These variations in atomic weight also left the possibility of unknown elements that, if discovered, might not fit into the table's periodic structure [2]. It was clear that atomic weight was not the defining characteristic of the elements, but nobody could confirm what else that might be.



Periodische Gesetzmässigkeit der Elemente nach Mendelejeff.

Reihen	Gruppe I R^2O	Gruppe II RO	Gruppe III R^2O^3	Gruppe IV RH^4 RO^2	Gruppe V RH^3 R^2O^5	Gruppe VI RH^2 RO^3	Gruppe VII RH R^2O^7	Gruppe VIII RO^4
1	H=1							
2	Li=7	Be=9,4	B=11	C=12	N=14	O=16	F=19	
3	Na=23	Mg=24	Al=27,3	Si=28	P=31	S=32	Cl=35,5	
4	K=39	Ca=40	Sc=44	Ti=48	V=51	Cr=52	Mn=55	Fe=56, Co=59 Ni=59, Cu=63
5	(Cu=63)	Zn=65	Ga=68	–=72	As=75	Se=79	Br=80	
6	Rb=85	Sr=87	Yt=88	Zr=90	Nb=94	Mo=96	–=100	Ru=104, Rh=104 Pd=106, Ag=108
7	(Ag=108)	Cd=112	In=113	Sn=118	Sb=122	Te=125	J=127	
8	Cs=133	Ba=137	Ce=137	La=139	–	Di=145?	–	– – – –
9	(–)	–	–	–	–	–	–	
10	– 165	– 169	Er=170	–173	Ta=182	W=184	–	Pt=194, Os=195(?) Ir=193, Au=196
11	(Au=196)	Hg=200	Tl=204	Pb=206	Bi=210	–	–	– – – –
12	–	–	–	Th=231	–	U=240	–	

The oldest periodic table chart discovered at the University of St Andrews in 2014. It is believed to be printed in 1885, constructed according to Mendeleev's periodic law. Highlighting the periodicity of chemical properties, the heavier cobalt (with an atomic mass of 58.9) appeared before nickel (58.7).

2014 年在聖安德魯斯大學發現最古老的元素週期表掛圖，相信是在 1885 年印刷，根據 Mendeleev 的週期定律而設計的，當中的排列強調元素特性的週期性，因此較重的鈷 (原子量為 58.9) 排在鎳 (58.7) 前。

The photo shows the replica of the St Andrews Periodic Table Chart displayed at HKUST, by permission of the School of Chemistry and Special Collections, the University of St Andrews.

圖為獲聖安德魯斯大學化學系及特藏組授權，展示在香港科技大學的聖安德魯斯元素週期表掛圖複製品。

Ernest Rutherford believed the solution might involve a new phenomenon called radioactivity, thanks to his experiments with radioactive decay. He assigned Henry Moseley, his new graduate student from Oxford, to study this phenomenon in 1910 [3]. But Moseley had other ideas. He has been following the developing field of X-rays closely ever since their discovery by Wilhelm Roentgen a decade earlier [4]. "Characteristic X-rays" of varying energy would be emitted when an element was struck by a stream of electrons. Moreover, the X-rays would be scattered through slightly different angles for each element used, and a technique to determine their wavelengths from this information had recently been developed by William and Lawrence Bragg [2]. This brought the intriguing problem of X-rays back within sight of the periodic table.

Moseley decided to extend this line of research and systematically measure the wavelengths of each element's characteristic X-rays. Returning to Oxford in 1913, he did this with a remarkably simple setup. By running a little train carrying samples of each element through a vacuum tube and then passing the line of fire of an electron beam, he was able to capture the positions of the emitted X-rays on photographic plates [1]. Knowing the angle by which they had been scattered, he could then calculate the wavelengths of the characteristic X-rays for each element. Moseley found that as the elements progressed up the periodic table, the scattered X-rays decreased in wavelength – and by taking the inverse square root of the wavelength, this relationship became a straight line [5].

This became known as Moseley's law, and Moseley could also explain how it came about. Two years earlier, Rutherford devised a model of the atomic structure: negatively charged electrons orbit a dense positively charged nucleus within the atom, with these charges cancelling each other out [5]. Moseley argued that the increasing size of this positive charge as atoms progressed up the periodic table would halt his electron beam more effectively, triggering a greater release of energy in the form of higher-frequency and lower-wavelength X-rays [2]. Because these positive charges could not be altered by chemical means, and were clearly a basic property of the atom, he suggested referring to them as "atomic numbers".

Thanks to this breakthrough, Moseley could now "call the roll" of the elements. If the X-ray wavelengths of two elements differed by a known minimum, there could be no other elements between them. From hydrogen to uranium there were exactly 92 elements, and it soon became obvious where the missing elements had to go. As Mendeleev had done, Moseley and others identified gaps at atomic numbers 43, 61, 72, 75, 85, 87 and 91, all of which were filled in the following 30 years [4]. The reversal of cobalt and nickel was also completely justified by cobalt's lower nuclear charge, the proper basis for its order in the table [4].

Henry Moseley had brought meaning to the order of the elements and set the periodic table on a firm foundation in the process, grounding it in a reality far deeper than the chemical and physical properties Mendeleev saw [4]. If anyone can be said to have "proved" the periodic table, it can only have been him.

在 20 世紀初，科學家還未知道應該如何歸納元素週期表。較舊的分類方法以遞增的原子量(atomic weight)把化學元素排列，而 Dmitri Mendeleev 的元素表則希望突顯元素特性的週期性，這又稱為週期定律，迫使他把原子量擱在一旁，成為次要的考慮因素 [1]。舉例說，鈷(cobalt)的原子量比鎳(nickel)大，但根據它們的化學特性，週期定律表明鈷應該排在鎳前面。這些原子量上的差別也對怎樣將新發現的元素納入既定的元素表造成困難 [2]。原子量顯然不是定義元素的恰當特性，但當時並沒有人能確定什麼才是。

Ernest Rutherford 從他的放射衰變實驗中取得靈感，相信答案可能涉及放射現象。在 1910 年，他把研究放射現象的工作分配了給從牛津大學來的新研究生 Henry Moseley [3]，但 Moseley 卻有其他想法。從十年前 Wilhelm Roentgen 發現 X 光起，

Moseley 一直密切留意著 X 光這個正在當時冒起的範疇 [4]。當一種元素被一連串電子撞擊時，會射出帶獨特能量的 X 光。此外，每種元素 X 光散射的角度都會稍稍不同，William 和 Lawrence Bragg 這對父子利用了這項資訊在不久之前發明出一項量度 X 光波長的技術 [2]，這把極具吸引力的 X 光課題帶到了元素表前。

Moseley 決定繼續這項研究，並有系統地量度每種元素獨有 X 光的波長。在 1913 年返回牛津大學後，他用非常簡單的裝置完成了量度。透過在真空管中移動一輛放著每種元素的小火車並使其穿過電子束，他成功使用照相底片記錄散射 X 光的位置 [1]。知道 X 光散射的角度後，他便可以計算出每種元素獨有 X 光的波長。Moseley 發現如果把元素按元素表的順序順著數，散射 X 光的波長就會隨之下降；透過取波長的反平方根，兩者的關係就會變成一直線 [5]。

這被稱為摩斯利定律（Moseley' s law），Moseley 還對其作出解釋。兩年前，Rutherford 提出了一個原子結構模型：在原子裡，帶負電的電子環繞著密度高而帶正電的原子核旋轉，這些電荷互相抵消 [5]。Moseley 指出原子的正電荷會隨著元素在元素表較後的位置而增加，這令較後的元素能更有效地使電子束停下，引發更多能量以較高頻率和較短波長的 X 光放出 [2]。由於這些正電荷不能透過化學方式被改變，又明顯地是原子的基本特性，他建議稱之為「原子序（atomic numbers）」。

這項突破性的發現使 Moseley 現在可以一個一個地替元素「點名」了。如果兩個元素的 X 光波長相差一個最小的已知值時，它們之間就可能沒有其他元素的存在。由氫（hydrogen）到鈾（uranium）剛好有 92 個元素，那些「失蹤」元素的蹤影現在無所遁形了。像 Mendeleev 之前的工作一樣，Moseley 和其他科學家找出了原子序 43、61、72、75、85、87 和 91 是未被填補的空隙，它們全部都在隨後 30 年被填補 [4]。鈷和鎳倒序的情況亦因為鈷有著較低核電荷這一點被完美解釋，核電荷因此成為了決定元素表裡排列次序的恰當根據 [4]。

Henry Moseley 為元素的排列賦予了意義，過程中亦把排列元素週期表背後的依據釐清，使其根據遠不止是停留在 Mendeleev 對化學和物理性質上的觀察 [4]。如果要說一個曾經「證明」元素表的人，那就非 Moseley 不是了。

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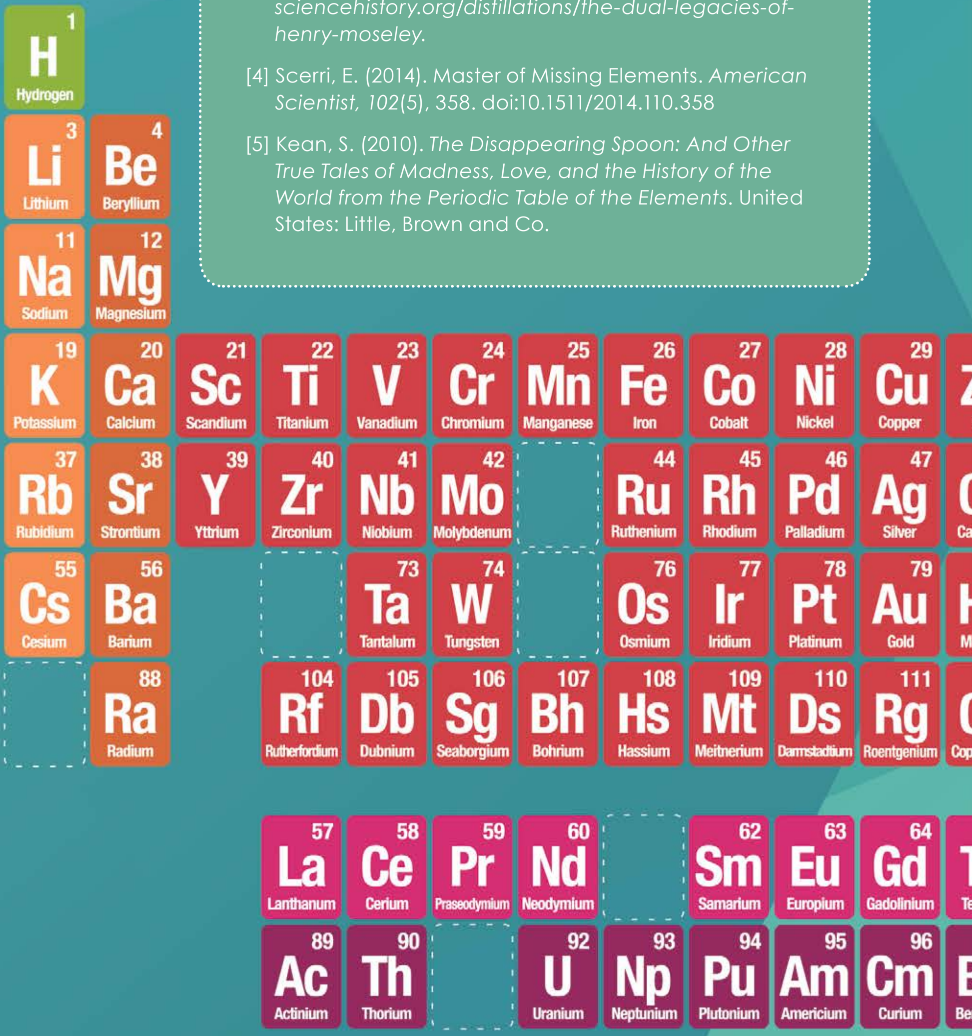
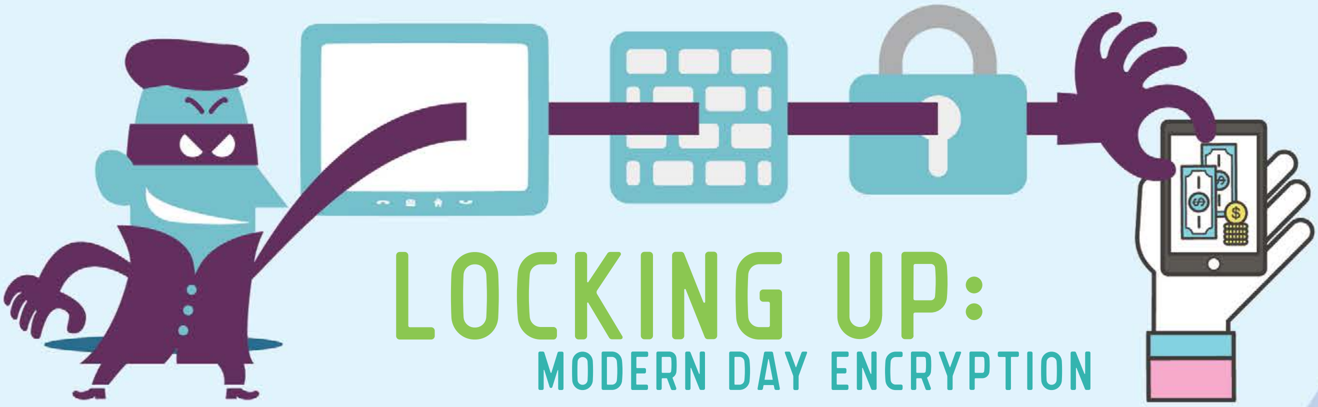


重門深鎖：現代密碼學

LOCKING UP:
MODERN DAY ENCRYPTION



By Sonia Choy 蔡蒨珩

The spat about WhatsApp's new user agreement has prompted another flurry of discussion of online security. We often see messages stating "this conversation is encrypted" – but how exactly does modern day encryption work, and how safe are we?

If you've been to an escape room, you've probably encountered a cipher or two – scrambled messages that you have to solve in order to escape. The best known of encryption methods is probably the Caesar cipher, dating back to the Romans, which shifts all the letters by a certain number of positions in the alphabetical order. Unfortunately, this is also the easiest cipher to break, because of something called frequency analysis. In English, certain characters occur most frequently; for example, at this point in the article (*), the letter "e" has appeared 81 times, more than any other letter. One can look at a Caesar cipher text and see which letter appears the most; it is then not very difficult to figure out the amount of shifting involved.

Thus began the evolution of ciphers; instead of shifting by one letter, people tried shifting with a so-called code word, then by sentences, using the so-called Vigenère cipher. This culminated in the famous Enigma, which basically amounts to a series of rather clever shifts, but that was also famously cracked during the Second World War by Alan Turing at Bletchley Park. When that happened, people realized that a new way of encryption was needed.

Enter RSA. Named after its inventors (footnote 1), Rivest, Shamir and Adleman, RSA is the main method of encryption in the modern day, but is fundamentally different from the ciphers I mentioned above. The difference lies in the types of keys used; while the Caesar cipher and Enigma both use symmetric keys, RSA is an example of asymmetric, or public key cryptography. In symmetric cryptography the key used to encrypt the message and decrypt the received message is the same; however, RSA makes use of two different keys, the public and private keys – the key locking up the box is not the same key used to unlock it! It all seems rather unintuitive at first, but the encryption actually relies on only two concepts – prime numbers and modular arithmetic.

Prime numbers are numbers greater than one that can only be divided by one and itself; they have been the subject of a previous article in *Science Focus* (Issue 020), and are very interesting in their own right. Primes can also get arbitrarily large – currently the largest known prime that we can actually write down has 24,862,048 digits. RSA encryption relies on the fact that factoring large numbers is generally very slow, even for people with enormous computing power, so breaking the code requires a huge amount of computing power that is simply not worth it (footnote 2).

Another technique is what mathematicians call modular arithmetic, which is, essentially, a generalization of telling the time. In 24-hour time system, we would tell the time modulo 24 – three hours after 23:00 is always 02:00 and never 26:00 (footnote 3). This is actually just division in disguise: to get the value of n mod a, just divide n by a enough times until you reach some value that is smaller than a – the remainder of our division is exactly the value we require.

With these two concepts in mind, the RSA algorithm is not too complicated – we'll break down the steps in some detail here [1].

To demonstrate, we pick two prime numbers, say $p = 11$ and $q = 13$. Multiply them together to get the public key $n = 143$. (In reality these primes are huge – the current recommendation is 2048 bits (footnote 4), but for the sanity of our editor, we'll keep them relatively small!) We also choose another number e which has no common factors, i.e. coprime, with 10 (i.e. $p - 1$) and 12 (i.e. $q - 1$); here we choose $e = 7$. The choice of n is unique for everyone, and e and n are known as the "public key". They are published in a public directory that computers can use when their owners want to send messages to each other.

Say Cliff wants to send me a very simple message – the most simple one possible – "Hi". As expected, if you want a computer to work, you have to turn letters into numbers. Thankfully, a system already exists – American Standard Code for Information Interchange (ASCII), which turns letters and symbols into 7-bit numbers, works just fine. In ASCII "H" is represented by the number 72, and "i" by the number 105.

To encrypt the letter "H", Cliff now has to find my public key. He reads from the directory that n = 143 and e = 7. The encrypted text is given by c = T^e (mod n). Here our text T_1 = 72, so the encrypted text is c_1 = 72^7 (mod 143), a very intimidating expression that seems impossible to compute by hand. But we can enlist the help of computers – and a quick Google reveals that c_1 = 19 (mod 143). So the first number we need to send is 19. We repeat the above procedure for the letter "i": c_2 = 105^7 (mod 143), so the second number is c_2 = 118 (mod 143). So the message "Hi" becomes "19 118".

To the outsider, it is impossible to recover the original message, since you cannot reverse your way from a modular number; however, you have one extra edge – the values of p and q – that sets you apart. Without them, you would need to factorize n, which is extremely time consuming since n is very large. The key to decryption is calculated from the following formula: take the least common multiple of p - 1 and q - 1, lcm (10, 12) = 60. The decryption key d is given by the following equation: 1 = (e x d) mod (lcm (p - 1, q - 1)). In our case, 1 = (7 x d) mod 60; so d = 43. This is our magical number to get back the message. And finally the decrypted message, m, is given by m = c^d (mod n). We have received two letters, so we will decrypt them separately: The first letter is 19^43 (mod 143), which gives us 72 (mod 143), the letter "H"; similarly, the letter "i" comes from 118^43 (mod 143) = 105 (mod 143). These look like calculations involving awfully large numbers, but computers can do them extremely easily. Also, with d, you can now decrypt every single message that Cliff sends you afterwards (footnote 5).

The encryption works because of a theorem known as Fermat's Little Theorem – although by the same person, it is not the infamous Fermat's Last Theorem. The theorem looks rather innocent at first sight: a^p ≡ a (mod p) for any prime p (footnote 6) – but is in fact key (pardon the pun) to why the encryption works, since the exponential features multiple times. The proof requires a bit of machinery that can be easily found on Wikipedia, and we will skip that for now.

Currently the RSA cryptosystem is seen as the default choice for encrypting small amounts of data, such as keys to symmetric key cryptography (footnote 7). The largest known factorized n is 250 digits long (829 bits), which took 2700 core years (footnote 8), and was factorized in 2019 [2]. The usual length used for encryption, in contrast, is 2048 bits, so we are still safe for the time being. However, history tells us that the codebreakers will always catch up – and we will need to find a new encryption method in the future.

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1 Actually, the first inventor of the RSA was Clifford Cocks, an English mathematician, who described the algorithm four years ahead (1973) of Rivest, Shamir and Adleman (1977); sadly, he worked for the British Intelligence Agency, and his work wasn't released until more than 20 years later in 1997, so RSA got all the credit.

2 That, however, may change with quantum computing, but at the moment quantum computers are not fast enough to hack RSA yet. If you're interested, try Googling "Shor's Algorithm".

3 There is a slight catch, however; in 12-hour time system, when telling the time we say 12 o'clock when the clock strikes twelve, but in modular arithmetic we say 12 ≡ 0 (mod 12) instead.

4 Bit is short for "binary (base 2) digit"– so a 7 bit number ranges from 1 to $2^7 - 1 = 127$, and 2048 bits range from 1 to $2^{2048} - 1$, around 617 digits.

5 The equation always has a unique solution d because we assumed that e is coprime with 10 and 12 from the beginning.

6 This equation is in modular arithmatic, not the algebra that most of us are familiar with. It actually means a^p (mod p) ≡ a (mod p).

7 RSA is the key (pun intended) component of the larger cryptographic protocol called TLS (Transport Layer Security), used for many online transactions and communication.

8 The term "core year" refers to the equivalent of using one CPU core continuously for a year (365 days). The author uses Intel Xeon Gold 6130 CPUs as a reference [2].

WhatsApp 的新使用者授權合約成為了前陣子的全城熱話，也再次引起了大家對網絡安全的討論。我們經常看到「此對話已進行端對端加密」之類的訊息 — 可是，你有想過現代的加密過程到底是怎樣運作的嗎？我們又有多安全？

如果你有玩過密室逃脫遊戲的話，你應該碰到過一兩組密碼（cipher）— 就是那些看似無意義的亂碼，然而你必先解開箇中玄機才能逃脫。最著名的加密法大概是羅馬帝國時代的凱撒加密法（Caesar cipher），它把所有字母都按字母排列順序偏移某個數值的位置。可是，凱撒密碼也是最容易解開的密碼，因為我們可以對其進行頻率分析。在英文裡有著幾個最常出現的字母，譬如在這篇文章的英文原文裡，英文字母「e」到此為止已出現了 81 次，比其他字母都要多。解密者可以看看凱撒密碼裡哪個字母出現次數最多，那就不難猜到原文被順移了多少個字母。

從此，不同的加密法陸續誕生。與其只將每個英文字母按一定數值的位置偏移，人們開始將字母根據一個字，甚至一段文字進行不同的偏移，稱為維吉尼亞密碼（Vigenère cipher）。不斷複雜化的加密法，最終造就了著名的恩尼格瑪密碼機（Enigma），它的基本上是一系列相當聰明的字母偏移。儘管複雜如此，也眾所周知地被 Alan Turing 在英國政府的解密基地—布萊切利園（Bletchley Park）破解了。這件事發生之後，大家都意識到發展嶄新加密法的需要。

然後是 RSA。它是現代加密的主要方法，以三位發明家 Rivest、Shamir 和 Adleman 的姓氏命名（註一）。RSA 加密演算法和以上提到的加密法有著本質上的不同，凱撒加密法和恩尼格瑪密碼機使用對稱金鑰（symmetric keys），

而 RSA 則是非對稱式加密（asymmetric cryptography）或公鑰加密（public key cryptography）的一員。在對稱式加密（symmetric cryptography）中，為訊息加密和解密用的金鑰是一樣的；但是 RSA 用上公鑰（public key）和私鑰（private key）兩把不同的金鑰 — 即是鎖上箱子用的鑰匙並不是解鎖的那把！加密和解密用上兩把不同鑰匙似乎難以用直覺理解，但 RSA 其實只依靠兩個基本概念：質數和模算數（modular arithmetic）。

質數是大於一而除了一和自己外，無法被其他自然數整除的數。它們本身就非常有趣，亦是我們曾經在第二十期討論過的課題之一。質數可以是任意大的：我們已知能寫出來的質數之中，最大的一個有多達 24,862,048 個數位。RSA 加密演算法就是利用因數分解通常是極費時這一點，即使擁有強大電腦力量的人亦然，因此要把加密內容破解往往需要花上不合理的電腦力量，令人敬而遠之（註二）。

另一個重要的概念是模算數。那基本上和從時鐘看時間差不多，在 24 小時制裡，我們會以「時間模 24（time modulo 24）」來描述小時 — 23:00 後的三個小時是 02:00，而不是 26:00（註三）。模算數的原理基本上就是除數：要得出 $n \bmod a$，基本上就要把 n 除以 a 約干次，直至商數比 a 小，得出的餘數就是我們要找的值。

理解了這兩個概念後，要明白 RSA 加密演算法其實不太難，在此我們會逐步解釋 [1]。

我們首先選兩個質數作示範，例如 $p = 11$、$q = 13$。把它們相乘，得出公鑰 $n = 143$。（在現實世界中這些質數都極為龐大，現在建議的是 2048 位元（註四）。可是為了編輯的身心健康著想，我們這次選了比較小的數值！）我們也要選一個與 10（即 $p - 1$）和 12（即 $q - 1$）沒有共同因數（互質）的數字 e，這次我們選 $e = 7$。每個人選的 n 都不同，而 e 和 n 就是剛才提到的公鑰，它們被發表在一個公開的目錄中，當傳送訊息給別人的時候，電腦可以使用目錄中的公鑰。

假設 Cliff 想給我傳一個非常簡單的訊息，越簡單越好 — 「Hi」。一如所料，如果你要電腦工作，就要先把英文字母轉成數字。很感恩，我們已經有一套這樣的系統 — 美國資訊交換標準代碼（American standard code for information interchange/ASCII），它可以將英文字母變成 7 位元的數字。在 ASCII 中「H」的代碼是 72，而「i」的代碼是 105。

要把字母「H」加密，Cliff 要找出我的公鑰。他從目錄得知 $n = 143$、$e = 7$。加密後的文字由公式 $c = T^e \pmod{n}$ 得出，我們的第一個字母是 $T_1 = 72$，經加密後會變成 $c_1 = 72^7 \pmod{143}$ — 這看起來很棘手，絕不是人手可以計算的，但我們可以借助電腦的力量 — Google 一下便可以得出 $c_1 = 19 \pmod{143}$，所以我們第一個要傳送的是 19。我們重複上述的步驟一次來加密「i」：$c_2 = 105^7 \pmod{143}$，因此第二個數字是 $c_2 = 118 \pmod{143}$。訊息「Hi」也就變成了「19 118」。

對外人來說，解開加密訊息是不可能的，因為你不能從已取模的數字還原本來的數字；可是，我們比外人知道多兩項資訊，就是 p 和 q 的數值。沒有了它們，你就要對 n 進行因數分解，而現實上 n 的數值很大，分解往往極之費時。解密的關鍵如下，我們先取 $p - 1$ 和 $q - 1$ 的最小公倍數 $\mathrm{lcm}(10, 12) = 60$，解密的金鑰 d 能從方程式 $1 = (e \times d) \bmod (\mathrm{lcm}(p - 1, q - 1))$ 得出。對我們而言，$1 = (7 \times d) \bmod 60$，所以 $d = 43$ — 這就是我們還原訊息的神奇密碼了。最後經過解密的訊息 m 可以由方程式 $m = c^d \pmod{n}$ 得出。我們收到了兩個字母，所以要把它們分開解密：第一個字母是 $19^{43} \pmod{143}$，等於 $72 \pmod{143}$，亦即是字母「H」；同樣地，字母「i」來自 $118^{43} \pmod{143} = 105 \pmod{143}$。這些計算看似涉及天文數字，但對電腦來說其實輕而易舉。此外，有了 d，你以後可以還原 Cliff 給你的每一條訊息（註五）。

RSA 加密法之所以會成功，是因為數論中的費馬小定理（Fermat's Little Theorem）— 就是那個費馬，可是這並不是把數學家弄得焦頭爛額的費馬最後定理（Fermat's Last Theorem）。費馬小定理乍看起來非常簡單：若 p 是質數，$a^p \equiv a \pmod{p}$（註六）。這可是 RSA 加密法的關鍵，因為 RSA 常常需要取 p 次方的計算。費馬小定理的證明需要花點筆墨才能解釋，但在維基百科也能輕易找到，這裡我們就不介紹了。

現在 RSA 加密系統是用於加密少量訊息的預設選擇，譬如用於加密對稱金鑰加密中的金鑰（註七）。現時已知最大被成功因數分解的 n 有 250 個數位（829 位元），電腦

用了 2700 核心年（註八）在 2019 年將其分解 [2]。相比之下，用於加密的長度一般為 2048 位元，因此我們暫時還是安全的。然而，從歷史上看，所有加密法都總有被人破解的一天，那時我們就要創造另外一種新的加密法了。

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1 其實第一個發明RSA的人是英國數學家Clifford Cocks，他在1973年已經研究出RSA，比Rivest、Shamir和Adleman在1977年的發明還要早四年。可是，Cocks當時在英國情報部門工作，研究屬於機密，因此要到20年後的1997年才對外公布，所以這演算法就以Rivest、Shamir和Adleman命名了。

2 隨著量子電腦的發展，這可能會改變。可是現在的量子電腦還沒有成熟到可以解開RSA加密的地步。如果你對這方面有興趣的話，可以搜尋一下「秀爾演算法（Shor's Algorithm）」。

3 稍微不同的地方是，我們會說午夜十二時為零時或十二時，但是數學模算數的世界裡，我們會說$12 \equiv 0 \pmod{12}$（即是零時，並非十二時）。

4 位元的英文「bit」是「binary digit（二進制數位）」的縮寫，因此7位元的數值範圍是從1到$2^7 - 1 = 127$，而2048位元的數值則是從1到$2^{2048} - 1$，那大概有617個數位左右。

5 這條方程永遠有唯一解d，是因為我們一開始就設定e與10和12互質。

6 這條方程是用模算數計算的，並非我們熟悉的代數式。要留意左右兩邊均需取模，即是$a^p \pmod{p} \equiv a \pmod{p}$。

7 RSA是通訊協定TLS（Transport Layer Security；傳輸層安全性協定）的重要部分，TLS很多時被用於網上交易和通訊。

8 核心年（core year）代表用一個中央處理器（CPU）核心持續運行一年（365天）。研究的作者使用Intel Xeon Gold 6130 CPUs作為參考 [2]。

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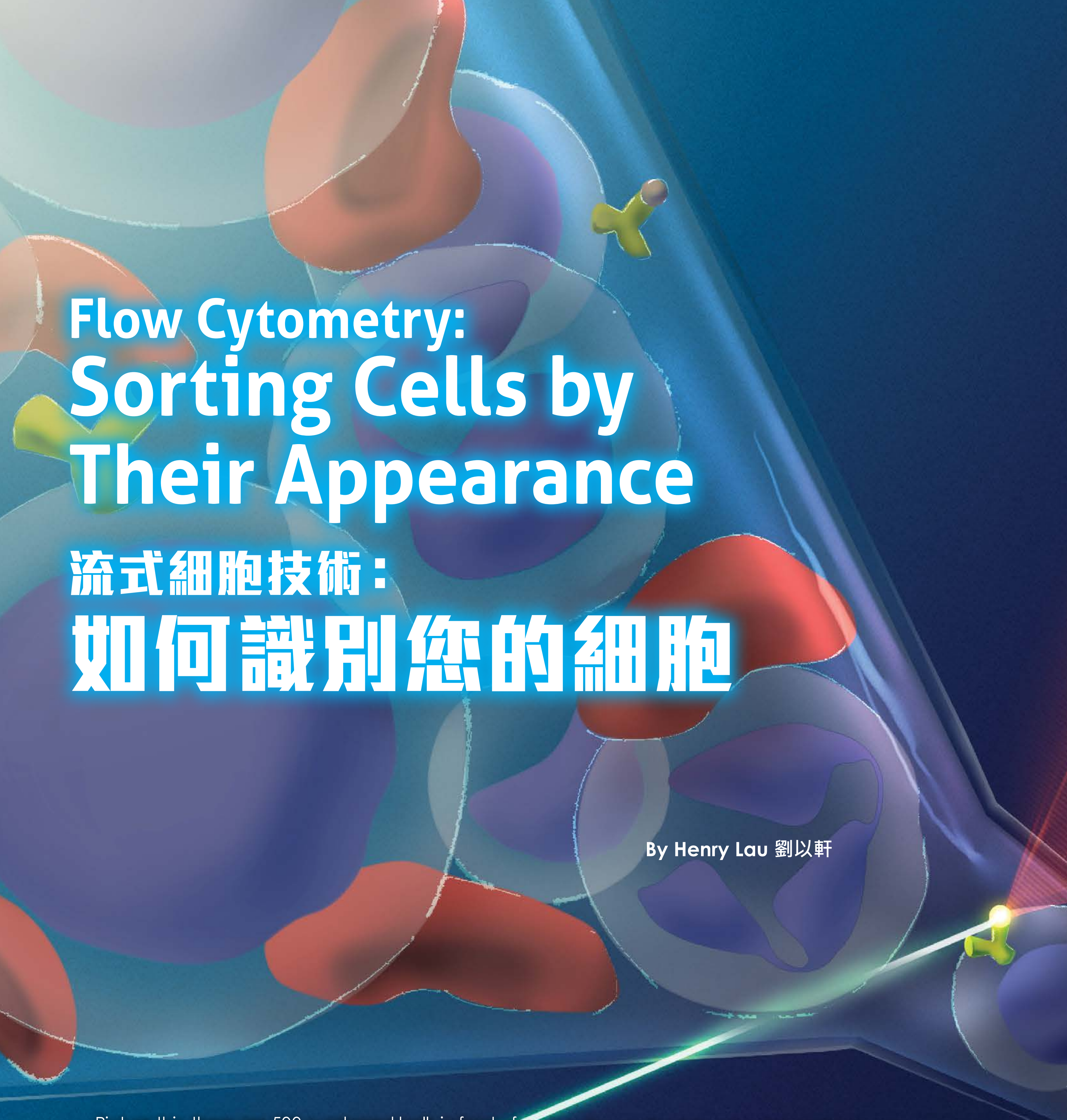
[2] Zimmermann, P. (2020, February 28). Factorization of RSA-250. Retrieved from *https://lists.gforge.inria.fr/pipermail/cado-nfs-discuss/2020-February/001166.html*



Flow Cytometry: Sorting Cells by Their Appearance

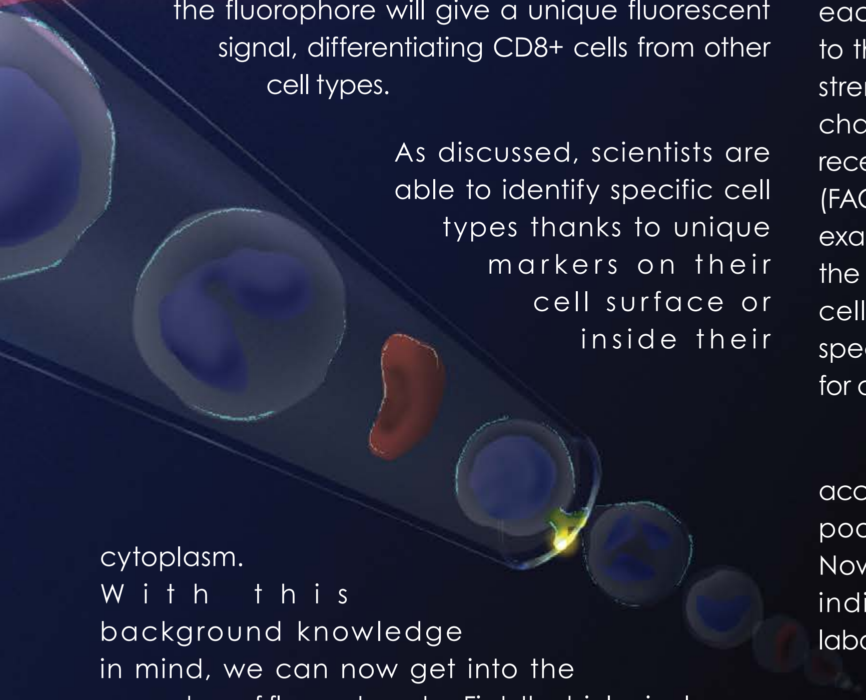
流式細胞技術：如何識別您的細胞

By Henry Lau 劉以軒

Picture this: there are 500 numbered balls in front of you. If you were asked to pick out the even-numbered balls in one second, how would you do so? To further complicate this, what if the balls were only 0.01mm in size, which is smaller than the width of a hair? How would you even begin to identify and sort these balls? Sounds like a trick question, doesn't it? The reality is, biologists have to deal with the same problem all the time. Only they're not handling balls, they're handling cells. Each of our organs are composed of many different types of cells. What if we are only interested in studying one type? The first step is to dissociate an organ into individual cells and "pick" the cells you like. The method to solve this problem was invented in the late 1960s [1], when biologists came up with an elegant solution to this riddle: flow cytometry.

Before we go into the mechanism of flow cytometry, we first have to understand the targets in question, namely the cells. Similar to how different people have unique identifying features, different cell types also have unique characteristics. The simplest identifying features of a cell are its relative size and complexity: some cells are larger than others and some cells have higher internal complexity (that is, having more cellular components like organelles or granules). Other than cell size and complexity, we can also identify cells by proteins that are preferentially produced by the cells. These proteins can either be positioned on the cell surface or sometimes contained within the cell's cytoplasm, like a transgenic fluorescent marker. With this in mind, as long as we are able to identify these features, we should be able to identify the cell type. For example, we can distinguish the two major types of mature T cells, helper T cells and killer T cells (a.k.a. CD4+ cells and CD8+ cells respectively), by figuring out which surface protein, CD4 or CD8, is expressed on the T cell (footnote 1).

The next question, of course, is how can we identify these cellular features? Size and complexity can be measured with lasers (more on that later), but unique protein markers are harder to identify. The solution to this comes from antibodies, which are proteins that can bind specifically to certain molecules. These antibodies can be selected such that they only bind proteins that are specific to certain cell types. These engineered antibodies are then joined (or conjugated) with unique fluorophores, which are chemical compounds that re-emits fluorescent signals at a longer wavelength upon excitation by a laser. Scientists can thus "label" the cells using these fluorophore-conjugated antibodies before the application of flow cytometry to identify the cell type. Using the example of mature T cells again, an engineered antibody-fluorophore conjugate, which can bind CD8 proteins on cell surfaces, will be able to stain CD8+ cells (killer T cells). Upon laser excitation, the fluorophore will give a unique fluorescent signal, differentiating CD8+ cells from other cell types.



As discussed, scientists are able to identify specific cell types thanks to unique markers on their cell surface or inside their cytoplasm. With this background knowledge in mind, we can now get into the procedure of flow cytometry. First, the biological sample in the form of a single-cell suspension (i.e. free-floating single cells in liquid medium; connected cells in a tissue need to be dissociated first) is loaded into the flow cytometer. The suspension is then focused into a single stream of liquid, like how water comes out of a tap in a single stream, whereupon cells will be arranged into a single file before passing through an array of lasers one by one. After that, an accompanying array of sensors will detect any signals that are subsequently generated. The photons in the laser beam will be able to pass through the liquid, in which the cells are suspended in, unobstructed but photons that encounter cells in the stream will be forced to divert from their original trajectory. Such divergence of light is known as scattering. Forward scatter, which measures the amount of light diffracted slightly due to contact with the cell membrane, can be used to give a measurement of the cell's relative size; the larger the cell, the more forward scatter there is [2, 3]. On the other hand, side scatter, which measures the amount of the light reflected at a greater angle upon contact with internal organelles or granules inside the cell, can give a measurement of the cell's relative internal complexity; the more objects there are inside the cell, the more side scatter there is [2, 3]. In addition, the lasers serve to excite any fluorophores conjugated to antibodies, allowing the labeled cells to be detected. With that, cells can be identified efficiently.

Besides identification, an extended function of flow cytometry is cell sorting. This is enabled by vibrating the stream of cells in the cytometer, causing the stream to break off into droplets containing mostly single cells. Then, the cell-containing droplets are each given different electrical charges according to their characteristics we tested before, such as the strength of fluorescence. The droplets with different charges will be deflected and sorted into different receptacles in the fluorescence-activated cell sorting (FACS) machine, so selected populations of cells, for example, successfully transformed cells that express the fluorescent marker, or tumor cells or white blood cells (including B cells and T cells) that express a specific surface protein marker [4], can be retained for analysis or further experiments.

Before the invention of flow cytometry, the accurate identification of specific cells from a diverse pool was almost impossible, let alone its isolation. Now, flow cytometry has become a common, yet indispensable technology in basic and clinical laboratories.

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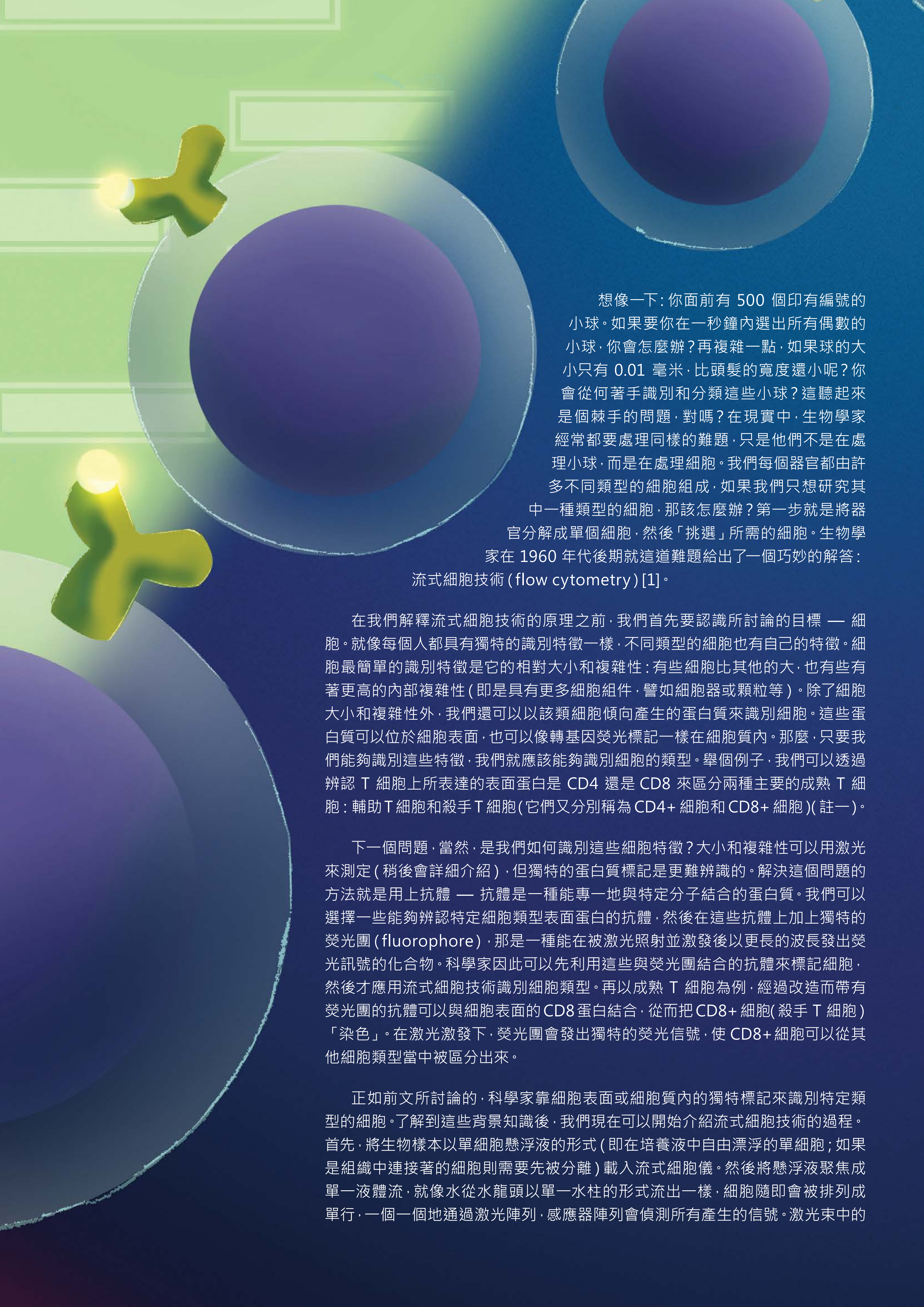
1 The HIV virus attacks CD4+ T cells.



想像一下：你面前有 500 個印有編號的小球。如果要你在一秒鐘內選出所有偶數的小球，你會怎麼辦？再複雜一點，如果球的大小只有 0.01 毫米，比頭髮的寬度還小呢？你會從何著手識別和分類這些小球？這聽起來是個棘手的問題，對嗎？在現實中，生物學家經常都要處理同樣的難題，只是他們不是在處理小球，而是在處理細胞。我們每個器官都由許多不同類型的細胞組成，如果我們只想研究其中一種類型的細胞，那該怎麼辦？第一步就是將器官分解成單個細胞，然後「挑選」所需的細胞。生物學家在 1960 年代後期就這道難題給出了一個巧妙的解答：流式細胞技術（flow cytometry）[1]。

在我們解釋流式細胞技術的原理之前，我們首先要認識所討論的目標 — 細胞。就像每個人都具有獨特的識別特徵一樣，不同類型的細胞也有自己的特徵。細胞最簡單的識別特徵是它的相對大小和複雜性：有些細胞比其他的大，也有些有著更高的內部複雜性（即是具有更多細胞組件，譬如細胞器或顆粒等）。除了細胞大小和複雜性外，我們還可以以該類細胞傾向產生的蛋白質來識別細胞。這些蛋白質可以位於細胞表面，也可以像轉基因熒光標記一樣在細胞質內。那麼，只要我們能夠識別這些特徵，我們就應該能夠識別細胞的類型。舉個例子，我們可以透過辨認 T 細胞上所表達的表面蛋白是 CD4 還是 CD8 來區分兩種主要的成熟 T 細胞：輔助 T 細胞和殺手 T 細胞（它們又分別稱為 CD4+ 細胞和 CD8+ 細胞）（註一）。

下一個問題，當然，是我們如何識別這些細胞特徵？大小和複雜性可以用激光來測定（稍後會詳細介紹），但獨特的蛋白質標記是更難辨識的。解決這個問題的方法就是用上抗體 — 抗體是一種能專一地與特定分子結合的蛋白質。我們可以選擇一些能夠辨認特定細胞類型表面蛋白的抗體，然後在這些抗體上加上獨特的熒光團（fluorophore），那是一種能在被激光照射並激發後以更長的波長發出熒光訊號的化合物。科學家因此可以先利用這些與熒光團結合的抗體來標記細胞，然後才應用流式細胞技術識別細胞類型。再以成熟 T 細胞為例，經過改造而帶有熒光團的抗體可以與細胞表面的 CD8 蛋白結合，從而把 CD8+ 細胞（殺手 T 細胞）「染色」。在激光激發下，熒光團會發出獨特的熒光信號，使 CD8+ 細胞可以從其他細胞類型當中被區分出來。

正如前文所討論的，科學家靠細胞表面或細胞質內的獨特標記來識別特定類型的細胞。了解到這些背景知識後，我們現在可以開始介紹流式細胞技術的過程。首先，將生物樣本以單細胞懸浮液的形式（即在培養液中自由漂浮的單細胞；如果是組織中連接著的細胞則需要先被分離）載入流式細胞儀。然後將懸浮液聚焦成單一液體流，就像水從水龍頭以單一水柱的形式流出一樣，細胞隨即會被排列成單行，一個一個地通過激光陣列，感應器陣列會偵測所有產生的信號。激光束中的

光子能不受阻礙地穿過細胞周圍的液體，但當遇到細胞時，光子會被迫偏離其原來的軌道，這種光的轉向稱為散射。前向散射（forward scatter）量度與細胞膜接觸後輕微繞射的光量，用於量度細胞的相對大小；細胞越大，前向散射越多 [2, 3]。另一方面，側向散射（side scatter）量度與細胞內部細胞器或顆粒接觸後以更大角度反射的光量，用作量度細胞相對的內部複雜性；細胞內的物體越多，側向散射就會越多 [2, 3]。此外，激光還可以激發與抗體結合的任何熒光團，讓我們能檢測到已標記的細胞。這樣，細胞就能被有效地識別了。

除了識別，流式細胞技術的一個擴展功能是細胞分類。這是通過振動細胞儀中的液體流，使液體分成大多只含有單個細胞的液滴而達成的。然後，我們根據之前測試過的細胞特性（例如熒光強度）賦予每個含有細胞的液滴不同的電荷。帶有不同電荷的液滴會在熒光流式細胞分選儀（fluorescence-activated cell sorting (FACS) machine）中轉向並進入機器內的不同容器，令目標細胞群可以被保留作分析或進一步實驗，這些細胞可以是成功轉化並表達熒光標記的細胞，或是表達某種蛋白標記的腫瘤細胞或白血細胞（包括 B 細胞和 T 細胞）[4]。

在流式細胞技術被發明之前，從含有各種各樣細胞的細胞群中準確識別特定細胞幾乎是不可能的事，更不用說把它們從中分離。現在，流式細胞技術已成為一般和臨床實驗室常見而不可或缺的技術。

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1 HIV 病毒攻擊 CD4+ T 細胞。

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