

times. That this person was given a deliberate burial in a cave when they died perhaps confirms that the care provided in life by this community continued after a person's death. Furthermore, there are signs of innovative behaviour in societies in this region of Borneo, namely, the creation of rock art 40,000 years ago⁶.

One limitation to this type of research is what is described as the 'osteological paradox' – survival for a suitably long period after an illness or its treatment is necessary before traces (whether healed or not) can be identified in ancient bones⁷. Ancient amputations are much rarer than, for example, signs of osteoarthritis. However, a reason why amputations are not often identified in skeletons might be that no healing occurred (unlike in this case), perhaps indicating that the person died as a result of the surgery. This discovery in Borneo is from a prehistoric time period, so no complementary texts are available to tell us about what care or treatment was available and practised at the time. Nevertheless, the evidence does tell us that some level of care must have been provided by this community.

Although the bones are in good condition, the remains are of a buried skeleton rather than of a whole preserved body. This makes it more difficult to interpret what care might have been given. The discussion about what types of care would have been needed to keep this child alive has to be based on assumptions, because we can never prove what happened. Nevertheless, a 'bioarchaeology of care' might be developed in the future to address such issues for this case in Borneo. This approach includes a set of steps called the Index of Care⁸ that can be used to assess whether a person with a disease or injury evident on their skeleton or in their soft tissues would need care to survive, and what might have been provided. It will be instructive to apply the index to this skeleton to gain a nuanced view of the specifics of the actual care that might have been necessary in this scenario.

What more could be studied? Taking a cross-section of the bone at the site of amputation and looking at it under a microscope would make it possible to identify diagnostic signs related to the healing of the bone using histological analysis⁹. Of course, healing can take place at different rates depending on aspects of a person's lifestyle (for example, malnourishment or infection might delay healing). This amputation is clearly well healed, and further microscopy would probably confirm the findings reported by Maloney and colleagues indicating that the amputation site healed well into what is called a resting state, and that the person survived for several years. This is a unique and ancient skeleton, and ethical considerations must apply to any analysis that would destroy bone in the process. Indeed, the information that might be

gained would not add much to the story.

The authors also observed a mix of male and female features in the skull and pelvis, and were therefore not able to estimate the sex of the individual. The sex of the child might have had implications for their treatment. Taking a bone sample to try to analyse ancient DNA might provide some clues to genetic aspects of the various factors that underlie biological sex, but we do not know whether any DNA is preserved, and it would again be a destructive analysis of a rare find.

A lot of anatomical and physiological knowledge is needed for surgery, and this was often gained through the butchering and dissection of animals in early societies where the dissection of human bodies might not have been an option. However, for this person in Borneo, we cannot know for certain whether the surgeon had that type of knowledge, or whether they had any insights into how to prevent blood loss or infection. Nevertheless, amputating part of the limb, including the foot, would have been no small undertaking, and it raises the question of how bleeding was controlled during and after the operation. Perhaps plant material, such as sphagnum moss, was used. We certainly have evidence of past and present communities using the medicinal and physical properties of natural resources to treat ailments, and it would have been essential for healing that the wound was kept clean after surgery to prevent infection.

There is no evidence of infection of the remaining part of the left leg. The amputation

is well healed, suggesting that if there had been an associated post-operative infection it was resolved. Of course, today a surgery-associated infection might be treated with antibiotics, but this treatment option would have been unavailable for the child if they needed treatment for infection.

Finally, whether the child had the use of an 'artificial limb' or a support (such as a crutch) could be contemplated. This has been considered for a sixth-century Austrian male individual who was excavated, although, in that case, there was archaeological evidence of an artificial foot preserved in the grave¹⁰.

Charlotte Ann Roberts is in the Department of Archaeology, Durham University, Durham DH1 3LE, UK.
e-mail: c.a.roberts@durham.ac.uk

1. Maloney, T. R. et al. *Nature* **609**, 547–551 (2022).
2. Buquet-Marcon, C., Philippe, C. & Anaick, S. *Nature Prec.* <https://doi.org/10.1038/npre.2007.1278.1> (2007).
3. Knüsel, C. J., Kemp, R. L. & Budd, P. J. *Archaeol. Sci.* **22**, 369–384 (1995).
4. Zhang, X. et al. *Int. J. Osteoarchaeol.* **32**, 132–141 (1995).
5. Tilley, L. *Int. J. Paleopathol.* **8**, 64–74 (2015).
6. Aubert, M. et al. *Nature* **564**, 254–257 (2018).
7. Wood, J. W., Milner, G. R., Harpending, H. C. & Weiss, K. M. *Curr. Anthropol.* **33**, 343–370 (1992).
8. Tilley, L. & Cameron, T. *Int. J. Paleopathol.* **6**, 5–9 (2014).
9. De Boer, H. H., van der Merwe, A. E. & Maat, G. J. R. *S. Afr. Archaeol. Soc. Goodwin Ser.* **11**, 52–60 (2013).
10. Binder, M. et al. *Int. J. Paleopathol.* **12**, 29–40 (2016).

The author declares no competing interests.
This article was published online on 7 September 2022.

Physical chemistry

Engineered molecules solve fluorescence issues

Juan-Carlos Sancho-García

The process by which pixels fluoresce in electronic displays uses energy highly inefficiently. The identification of fluorescent molecules with an unusual order of excited states opens up a fresh approach to tackling this issue. See p.502

Are you reading this News & Views article on a mobile phone? Do you stream your favourite series on a bright, flat-screen television, or help your kids do schoolwork on their tablets? If so, then one day you might benefit from the advance reported by Aizawa *et al.*¹ on page 502. They describe a breakthrough that overcomes long-standing constraints imposed by the laws of quantum mechanics on the energy efficiency of electronic displays, using a new strategy for understanding and engineering the interactions of light with matter.

When you flip a coin, the statistical probability of achieving either heads or tails is 50% when averaged over many trials, but the distribution of outcomes can vary for a small number of flips. Things are very different in the molecular world, because of the rules of quantum mechanics. Consider the physical process that produces fluorescence: an energy input puts a molecule into either a 'heads' or a 'tails' state (known as singlet and triplet states, respectively), with each state corresponding to a different energy of the molecule (Fig. 1a).

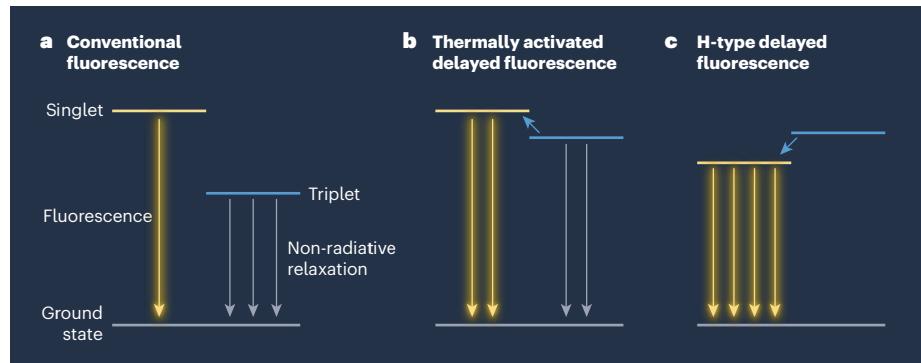


Figure 1 | Inverted excited states boost energy conversion in fluorescence. **a**, In conventional fluorescence, an energy input (not shown) induces molecules to populate either a singlet or a triplet state. Singlets relax to the ground state through fluorescence (emission of a photon), whereas triplets relax in a non-radiative manner (no emission). Because triplets form 75% of the time, and singlets just 25% of the time, only 25% of the energy input is converted into fluorescence. **b**, In thermally activated delayed fluorescence, the energy difference between the excited states is reduced to almost zero. Ambient thermal energy promotes the conversion of triplets to singlets, and so more molecules populate the singlet state than in **a**, increasing the fluorescence. **c**, Aizawa *et al.*¹ report H-type delayed fluorescence. In this case, triplets are higher in energy than singlets, so that there is no energy barrier to conversion. Theoretically, all of the molecules can fluoresce, regardless of which excited state they initially enter, improving the energy efficiency to 100%.

In this case, the chances of getting tails are much higher than the chances of getting heads – the probabilities are 75% and 25%, respectively – and the ratio of outcomes is always the same, regardless of the number of trials.

Only the molecules in the heads state can retain the energy and transform it into light, which is emitted as fluorescence in the red-to-blue region of the visible spectrum. By contrast, the molecules in the tails state immediately release the energy received to the environment, without producing light. The statistics of the ‘flipping’ process therefore imply that energy will be lost 75% of the time – or, to put it another way, the efficiency of light production from this physical process can never exceed an intrinsic limit of 25%.

What does this have to do with electronic displays? When triggered by the injection of charge from the battery, each of the pixels in a display lights up with a specific colour that originates from the physical process that produces fluorescence. The colour is a stream of photons of a particular wavelength, and can be emitted from only the 25% of the molecules in the pixels that adopt the heads state after charge injection.

Finding ways to improve the efficiency of this emission process has been a subject of research for the past few decades^{2,3}. Two main strategies have been pursued. The first involves introducing heavy atoms into molecules so that some molecules in the tails state can also emit light. The second approach aims to greatly reduce the energy difference between the heads state and the lower-energy tails state (Fig. 1b). Ambient thermal energy can then overcome the energy barrier between the two, thereby converting some of the tails to light-emitting heads. An energy-absorbing process such as this is said to be endothermic.

Aizawa *et al.* took a different approach. They aimed to find molecules for which the heads state is lower in energy than the tails state, rather than the other way around (Fig. 1c). In this case, instead of the molecules in the tails state just losing their energy, they can donate it to the lower-energy molecules in the heads state without needing to overcome any energy barrier, thus allowing the heads molecules to emit light. Theoretically, this could enable fluorescence with 100% energy efficiency – a goal that quantum mechanics suggests is challenging to achieve⁴, and which has so far been elusive in experiments.

If an energy-releasing (exothermic) process such as this could replace the current endothermic ones, it would not only enable the development of brighter screens, among other

The results suggest that the prospects for practical applications – possibly even in the immediate future – are excellent.

technological applications, but also reduce the energy consumption of such electronic devices. This, in turn, would decrease global energy demands and the associated carbon emissions – and could therefore be an asset in helping the world to meet the United Nations Sustainable Development Goals (<https://sdgs.un.org/goals>).

Previous calculations^{5–8} have predicted that an endo- to exothermic transformation is possible, notably for a family of triangular molecules called heptazines, and for structurally related molecules. Some experimental

evidence for this has also been reported^{9,10}. Aizawa *et al.* now present experimental evidence of heptazine molecules that can transform most of the injected energy into emitted light because the heads state is lower in energy than the tails state (that is, because the order of energies has been reversed).

The authors began their study by computationally screening a pool of 34,596 molecules to identify candidates that have a profile of excited states that would enable the desired exothermic fluorescence mechanism. They narrowed down the set of candidates to about 3% of the original number by focusing on those that would emit blue light (the most challenging colour to obtain by emission from organic molecules). They then selected two molecules that could be synthesized in the laboratory for experimental analysis.

It has always been difficult to determine whether fluorescence is produced only from molecules that are excited directly into the heads state, or whether it is also produced from molecules that are indirectly excited to the heads state through the tails state. Aizawa and colleagues used a variety of techniques in numerous experiments to assess this for their two molecules. They show convincingly that the order of energies for these states is indeed reversed for one of these molecules, and for some closely related ones. The authors name this mechanism of light emission heptazine-type (H-type) delayed fluorescence, to distinguish it from previously reported mechanisms.

Moreover, the authors show that the energy efficiency and colour quality of these emitters can be attained not only in small-scale laboratory experiments, but also at larger scales in commonly used electronic devices such as organic light-emitting diodes. This suggests that the prospects for practical applications – possibly even in the immediate future – are excellent. Overall, the authors’ findings introduce a new concept in light-matter experiments: the use of molecular engineering to overcome limitations previously thought to apply to all visible-light emitters.

The findings raise several questions. How many other molecules behave like those discovered by Aizawa *et al.*, challenging the rules of quantum mechanics? Why do only some molecules do this, and what is the physical basis for such behaviour? And will it be possible to find molecules that emit the other primary colours (red and green) needed for pixels in displays?

With respect to the development of emitters for practical applications, the next step will be to identify the molecular features that underlie this behaviour¹¹, so that libraries of compounds can be designed starting from computational screening. It will then be interesting to see how many of those molecules can be synthesized with high yield and purity, and

what the stability and lifetimes of the resulting electronic devices will be. The answers to these questions will determine whether, and how quickly, the technology can be adopted for use in everyday electronic devices.

Juan-Carlos Sancho-García is in the Department of Physical Chemistry, University of Alicante, E-03080 Alicante, Spain.
e-mail: jc.sancho@ua.es

1. Aizawa, N. et al. *Nature* **609**, 502–506 (2022).
2. Uoyama, H., Goushi, K., Shizu, K., Nomura, H. & Adachi, C. *Nature* **492**, 234–238 (2012).

3. Hatakeyama, T. et al. *Adv. Mater.* **28**, 2777–2781 (2016).
4. Sobolewski, A. L. & Domcke, W. *J. Phys. Chem. Lett.* **12**, 6852–6860 (2021).
5. de Silva, P. J. *J. Phys. Chem. A* **103**, 5674–5679 (2019).
6. Ehrmaier, J. et al. *J. Phys. Chem. A* **123**, 8099–8108 (2019).
7. Ricci, G., San-Fabián, E., Olivier, Y. & Sancho-García, J. C. *ChemPhysChem* **22**, 553–560 (2021).
8. Pollice, R., Friederich, P., Lavigne, C., dos Passos Gomes, G. & Aspuru-Guzik, A. *Matter* **4**, 1654–1682 (2021).
9. Leupin, W. & Wirz, J. *J. Am. Chem. Soc.* **102**, 6068–6075 (1980).
10. Leupin, W., Magde, D., Persy, G. & Wirz, J. *J. Am. Chem. Soc.* **108**, 17–22 (1986).
11. Ricci, G., Sancho-García, J.-C. & Olivier, Y. *J. Mater. Chem. C* <https://doi.org/10.1039/D2TC02508F> (2022).

The author declares no competing interests.

Plant science

An auxin-binding protein resurfaces after deep dive

Angus S. Murphy & Wendy A. Peer

The hormone auxin regulates plant growth through nuclear co-receptors. A rapid response also occurs at the cell surface after auxin is perceived by the receptor TMK1 and a co-receptor protein. Is ABP1 this co-receptor? See p.575

The plant hormone auxin exists in different forms, of which the most common is indole-3-acetic acid (IAA). Auxin regulates a range of crucial plant processes, including embryo development, organ formation, the branching of side shoots from the main stem, and directed (tropic) growth in response to stimuli such as light or gravity. Friml *et al.*¹ offer fresh insights on page 575 into how auxin is perceived at the cell surface. This process involves a receptor that mediates a signalling response, and a co-receptor protein that binds to auxin and also to the signal-mediating receptor.

Most aspects of auxin signalling involve a well-characterized mechanism in the cell nucleus. In the resting state in the absence of auxin, AUX/IAA proteins (which can function as auxin co-receptors) bind to proteins called ARFs to repress transcription of a set of genes. Auxin synthesized in the cell or transported from elsewhere promotes the association of AUX/IAA proteins with a receptor protein of the TIR/AFB family (TIR1, AFB1, AFB2, AFB3 or AFB4) to initiate a process leading to degradation of the AUX/IAA proteins. The result is derepression of ARF-dependent gene transcription to activate auxin-dependent gene expression.

However, some auxin responses, most notably those that rapidly activate cell expansion and auxin movement by activating proton pumps called H⁺-ATPases in the cell membrane, seem to be at least partially

independent of this system involving nuclear co-receptors. A decrease in electrical potentials at the cell membrane and an influx of calcium ions occur within seconds of IAA application. These processes depend both on the protein AUX1, which enables auxin import, and on intracellular TIR1/AFB receptors². Auxin inhibition of root growth in response to gravity

occurs by a mechanism³ that is independent of the mechanism that Friml *et al.* propose. Other phenomena, such as auxin-dependent regeneration of the fluid-conducting vascular tissue after wounding, are residually present in mutants of the plant *Arabidopsis thaliana* that lack components of the TIR1/AFB system.

For 50 years, the main candidate co-receptor for auxin on the surface of cells has been auxin-binding protein 1 (ABP1), which was discovered in maize (corn) and subsequently identified in many other plant species. However, inconsistencies in the evidence relating to its co-receptor status have generated scepticism about its role in relation to auxin. (See ref. 4 for an in-depth discussion of ABP1 function. Written by a researcher who has spent much of the past 35 years studying the structure and function of ABP1, it offers an excellent summary of the settled and unsettling history of ABP1 research.)

It is generally accepted that ABP1 contains an amino-acid sequence that targets it for residency in the endoplasmic reticulum, an organelle in which IAA, versions of IAA called IAA-amido conjugates and ABP1 are abundant⁵. ABP1 can bind strongly to an artificial, membrane-permeable auxin called NAA and to a ‘minor’ natural auxin, phenylacetic acid, under acidic conditions, comparable to those that exist in extracellular regions (the cell wall and the cell surface). However, despite being almost exclusively localized to the endoplasmic reticulum, ABP1 does not bind strongly to these molecules at the neutral pH characteristic of that organelle⁶. Another reason for ABP1 not being considered an auxin co-receptor is that a ‘loss of function’ mutation of the gene encoding ABP1 is not associated

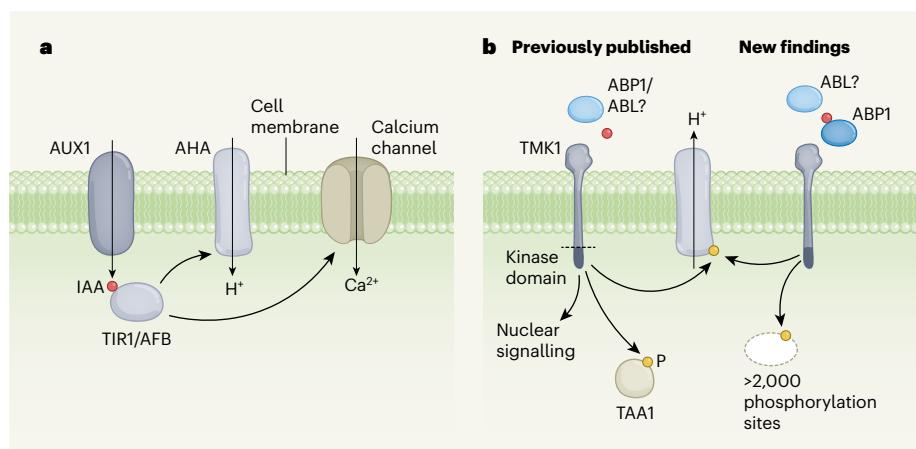


Figure 1 | A role for ABP1 in an auxin-mediated pathway. **a**, Auxin (IAA) enters cells through the protein AUX1 and binds to a protein of the TIR1/AFB family. This leads to rapid ion flow (within seconds) through the protein AHA and a calcium channel. **b**, Auxin is also perceived at the cell membrane by the receptor protein TMK1. Some aspects of this system were known, but whether the protein ABP1 or proteins of the ABP1-like (ABL) family act as a co-receptor that binds to TMK1 and auxin was unknown. TMK1 has a kinase domain that enables it to add phosphate groups (P) to target proteins¹⁰ such as TAA1 or AHA. When cleaved from TMK1, the kinase domain moves to the nucleus and stabilizes two proteins that repress transcription (not shown). Friml *et al.*¹ report that ABP1 is a co-receptor for TMK1. ABL proteins might have a role, too. The authors report a large number of sites that are phosphorylated when TMK1 and ABP1 interact.