that intracellular receptors engaged by DMT are involved in rapidly enhancing structural neuroplasticity, specifically increased dendritic growth and spine density, relative to membrane-localized receptors (see the figure). Bestowing cortical neurons in vivo with serotonin transporters allowed serotonin to access the intracellular receptors, mimicking the changes in structural neuroplasticity that are observed when cells were treated with DMT. The relevance of this phenomenon to changes in mouse behavior was assessed using a forced swim test (FST), a widely used approach that is thought to have predictive value of antidepressant effects in humans, although the actual clinical predictive validity is questionable (*11*). Providing serotonin access to intracellular 5-HT2ARs reduced immobility in the FST, which is considered an antidepressant-like effect. Given that serotonin cannot normally access intracellular 5-HT2ARs in cortical excitatory neurons owing to a lack of serotonin transporters, a role of endogenous DMT may be to engage the intracellular receptor pool and facilitate neuroplastic changes. Further assessment of the role of this mechanism in mediating circuit activity and resulting behaviors relevant to depression is necessary.

The lifetime prevalence of depression is ~20%, and it is a leading cause of disability worldwide. First-line treatments such as selective serotonin reuptake inhibitors are taken daily for weeks before therapeutic effects are potentially observed and lead to sustained remission in only ~30% of cases; they also have side effects that affect patient adherence (*12*). This has led to a shift in the search for depression therapeutics in favor of rapid-acting compounds such as ketamine, which can result in sustained therapeutic effects for days or longer after a single dose (*13*). Similarly, recent clinical trials have suggested that DMT and psilocybin are rapidly efficacious in treating major depression, with psilocybin appearing to have sustained therapeutic effects for weeks after treatment sessions that consist of a combination of psilocybin with supportive therapy (*2*, *3*).

Unfortunately, clinical trials with psychedelics are commonly statistically underpowered and mostly do not represent common patient populations. Moreover, it is impossible to adequately include a placebo control given the profound effects that these compounds have on perception, which can easily unblind both study participants and experimenters (*6*, *7*). As a result, it is difficult to predict how the existing clinical findings will be extrapolated to a wider population. Thus, psychedelic-assisted therapy should be embraced with cautious optimism; although the thousands of years of human psychedelic use and the positive outcomes of modern, though early stage, clinical trials point toward therapeutic potential, scaling psychedelic use to potentially millions of people with depression, for example, requires a careful and rigorous scientific approach.

The study conducted by Vargas *et al.* is a key achievement in the understanding of the mechanism of action of psychedelics. However, much needs to be done to affirm the sufficiency of signaling through intracellular 5-HT2ARs as mediators of the properties in humans, either hallucinogenic or medical, and to determine whether positive therapeutic outcomes can be separated from the classical psychedelic properties of such drugs. This will require interrogation of the specific signaling cascades engaged by intracellular 5-HT2ARs that lead to increased dendritic growth and spine density and defining the mechanistic relationship of such changes to cognitive processes. Moreover, understanding whether the findings for DMT are fully shared with all psychedelics (such as the structurally dissimilar mescaline), which was only partially explored by Vargas *et al.*, will be needed before the proposed mechanism can be described as a common psychedelic mechanism. Nevertheless, these findings are an important step forward for a rapidly expanding and much-needed field of study. ■

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PHYSIOLOGY

Photonic tinkering in the open ocean

Light-manipulating materials are discovered in the eyeglitter of pelagic crustaceans

By **Kate Feller** *and* **Megan Porter**

Billions of animals living in open water, or pelagic habitats, can disappear into their surroundings using a variety of light-manipulating camouflage solutions. These include transparent, antireflection, and glittery reflective structures. Although such photonic camouflage allows these animals to vanish into their surroundings, they still need to eat (and avoid being eaten), which requires the ability to detect their invisible neighbors. Thus, an arms race exists between predators and prey for the ability to see and yet not be seen (*1*). Evolutionary tinkering across the diversity of pelagic animals has produced multiple solutions for controlling the transmission, reflection, and detection of light. On page 695 of this issue, Shavit *et al.* (*2*) report the discovery of photonic glass materials that form the basis of sparkly "eyeglitter" in the larvae of pelagic crustaceans and allows for both reflective camouflage and vision. These findings present a mechanism for producing salient, tunable coloration and light manipulation in space-limited tissues.

When peering into a bucket of seawater scooped from the ocean, the tiny animals and larvae that live in open water, or zooplankton, often can only be spotted by their pigmented eyes. These black dots travel side by side through the water, giving no indication that they are part of a much larger creature. This is because the bodies of many crustacean zooplankton are almost as transparent as glass. This is achieved both through lack of pigmentation in most body tissues and by photonically minimizing the amount of light scattered or reflected from internal and external structures. How internal structures such as muscles, organs, and blood become transparent is still an open investigation, al-

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though internal transparency is sometimes an actively maintained, physiological process. For example, a loss of transparency can occur after repeated activity or stress and be regained after a brief rest (*3*).

In contrast to internal transparency, external transparency of pelagic crustacean cuticles (exoskeleton surface) is achieved with static physical structures. Tiny bumps, or nanoprotuberances, covering the animal's surfaces serve to minimize reflections or glare that would make them more noticeable. In just one group of pelagic arthropods, the hyperiid amphipods, up to four variations of these antireflecting structures have been identified (*3*). Because transparent camouflage is under strong selection, convergent evolution has likely devised additional photonic solutions that are yet to be described.

Although it is an effective camouflage, total body transparency is not possible in animals that require vision. For eyes to properly detect a visual scene, the light-sensing cells must be isolated from one another by dark pigments. This explains why the eyes of crustacean zooplankton are so easy to spot when viewed in a bucket of seawater. Larvae of several groups of crustaceans have independently evolved a solution to this dilemma: reflective camouflage. The dark bits of the eyes are enveloped with a sparkly eyeglitter—photonic structures that reflect light matched to the color of the surrounding water (*4*).

Shavit *et al.* delve into the chemical and structural basis of eyeglitter camouflage in larvae of the freshwater shrimp *Machrobrachium rosenbergi*. They found a previously unknown type of compact, photonic glass formed by nanospheres in the eyeglitter structure that are smaller than the wavelengths of visible light (400 to 750 nm). This newly discovered material is tunable and can reflect colors ranging from deep blue to yellow, depending on the camouflage needs of the animal at different depths and times of day. Even more intriguing, they found that the glittery eyeshine of two additional groups of crustacean larvae (decapod crabs and stomatopods, or mantis shrimp) appear to arise from similar nanosphere assemblies, although through the use of a different crystalline material that remains to be identified. This suggests that different lineages have evolved convergent mechanisms to cloak the dark retina from view. These discoveries highlight the vast potential of crustacean zooplankton for discovery of photonic materials that either reflect or transmit light in ways that can render objects invisible.

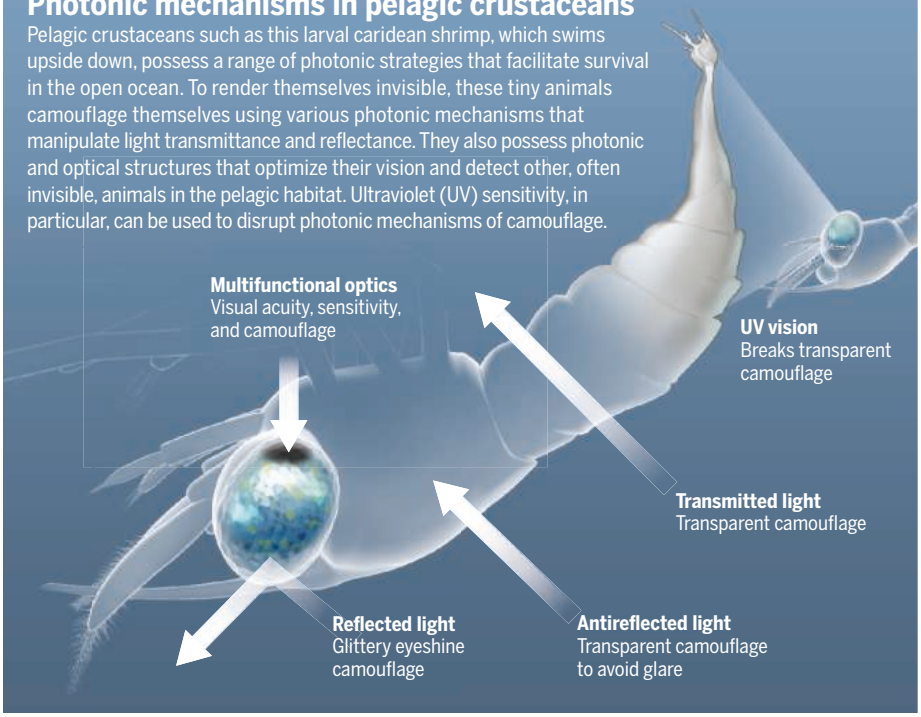
In the game of open-ocean hide and seek, animals also possess eyes that are specialized to meet their visual needs without compromising invisibility. In the study of Shavit *et al.*, the same reflective structures in *M. rosenbergi* used for eyeshine may play an additional role in enhancing visual sensitivity in the dark or isolating photoreceptors for improved resolution. Given their presence in other larvae, multifunctional reflective structures seem to be a common theme within such tiny eyes. For example, reflecting structures inside mantis shrimp larval photoreceptors filter light arriving at some photoreceptors, while reflecting light to enhance the sensitivity of other cells (*5*).

Another emerging theme in the visual ecology of small, pelagic crustaceans is the prevalence of ultraviolet (UV) sensitivity. UV light scatters more than visible wavelengths, even in the most transparent tissues. Thus, this scattering can make an animal appear as a shadow against the background of open water when viewed in the UV range, effectively breaking transparent or reflective camouflage (*1*). Although molecular, physiological, and anatomical studies of pelagic crustacean vision are still in their infancy, larvae of some mantis shrimp larvae (*Neogonodactylus oerstedii*) may take this invisibility-detecting strategy to the extreme because they have photoreceptors with the capability of detecting up to three distinct wavelengths of UV light (*6*). Further examination of open water crustacean visual systems may reveal innovative multifunctional optical solutions for both sensing and manipulating light, particularly UV wavelengths (see the figure).

Why are such exciting photonic discoveries only being made now? The vastness of the pelagic realm, and the relatively sparse distribution of animals within it, makes this habitat difficult to access and sample effectively (*1*). Larval crustaceans are numerous and easier to collect than larger pelagic species, yet they remain understudied owing to an historic lack of descriptions that link larval stages to the adult form for identification. The development of DNA barcoding to molecularly identify crustacean larvae has allowed species level comparisons like never before, especially for the study of biological photonics (*4*–*6*). The diversity of optical solutions discovered in just a few recently investigated pelagic crustaceans spotlights the untapped potential for photonic innovation yet to be found in animals living in the open ocean. By mimicking nature's solutions, humans can optimize and develop better photonic materials for solar energy, communications, remote sensing, and other light-dependent technologies. Given the diverse applications of photonics, studies of how these minute creatures both hide and seek in the open ocean is a burgeoning resource of bioinspiration for human detection, control, and manipulation of light. ■

Photonic mechanisms in pelagic crustaceans

Pelagic crustaceans such as this larval caridean shrimp, which swims upside down, possess a range of photonic strategies that facilitate survival in the open ocean. To render themselves invisible, these tiny animals camouflage themselves using various photonic mechanisms that manipulate light transmittance and reflectance. They also possess photonic and optical structures that optimize their vision and detect other, often invisible, animals in the pelagic habitat. Ultraviolet (UV) sensitivity, in particular, can be used to disrupt photonic mechanisms of camouflage.



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