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Opinion

From grown to programmed: Optogenetic control of bioactive composition in plants

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1 From a Nobel prize to a plant problem

The 2026 Nobel Prize in Physiology or Medicine recognized discoveries concerning light-gated ion channels and optogenetics. A landmark 2005 study showed that channelrhodopsin-2 could control neural activity with millisecond precision. This work proved one concept. Light can serve as a precise and programmable switch for specific cellular processes.

For most people, light and plants simply mean photosynthesis. Plants use light to acquire energy. But for medicinal and edible plants, can light become a defined input for controlling bioactive composition? Native light regulation has already given us a positive answer. Mulberry stays poor in flavonoids indoors until a low-dose ultraviolet-B (UV-B) supplement arrives[1]. Chinese bayberry raises quercetin only when UV-B reaches it[2]. *Dendrobium officinale* shifts its flavonoids and polysaccharides with the light level[3]. These examples show that light shapes plant composition. But they also point to a fundamental weakness. Native light regulation is inherently systemic. It cannot precisely tune a single target.

To overcome this lack of target specificity, we need a method with a fundamentally different logic. If native light regulation nudges the plant's own photoreceptors and relies on its inherent networks, it asks the plant a question in its own language. Then optogenetics introduces an exogenous light-sensitive switch. We wire this switch directly to a chosen gene. It creates an independent control channel to drive that gene on demand. Conventional agronomy relies entirely on the first approach. It treats light as a continuous, fluctuating environmental input. We measure it, we shade it, and we hope for the best. But this approach only tunes the average, whole-plant condition. It cannot provide a discrete control channel to switch on one specific gene without disturbing the rest of the network. The industrial problem persists: We keep turning a continuous environmental knob without a direct, targeted dial.

2 What light actually does in a leaf?

A plant has no eyes, but it has light receptors. Think of them as antennae. Each antenna is tuned to a specific wavelength. When the right light arrives, the receptor changes shape. This shape change sets off a direct chain of events in the nucleus.

UV-B provides the cleanest example. In the dark, the UV-B receptor UV RESISTANCE LOCUS 8 (UVR8) exists as a paired unit. UV-B absorption causes the pair to split into single units. The single UVR8 binds a protein called COP1. In darkness, COP1 marks the transcription factor HY5 for degradation. When UVR8 binds COP1, that degradation stops. HY5 accumulates, enters the nucleus, and activates the genes for flavonoid synthesis, such as *CHS*, *F3H*, and *FLS*[4].

Different wavelengths trigger different photoreceptors. Each receptor triggers a specific transcription program. The activated photoreceptor releases a signal that integrates into the plant's endogenous network. The response is coordinated by the plant's own physiological logic, across multiple tissues and metabolic pathways. This is different from the textbook picture of chemical signaling. A hormone or a drug binds a receptor, and the receptor passes a signal along. The chemical is consumed or cleared, and

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the signal fades. Light is not consumed. The switch stays on as long as light is present, and it reverses when light is removed. That makes light a controllable input.

3 What native light regulation cannot do?

Native light regulation is powerful, but it cannot serve as a programmable input. Its systemic nature leads to three specific failures. Each failure reveals a gap that only optogenetics can fill.

The first limitation is causal ambiguity. Consider mulberry. A low dose of UV-B reroutes carbon into flavonoids[1]. But the mechanism is a broad sweep. Transcriptomic changes show that auxin and jasmonate signaling are both implicated. This signaling shift alters multiple biosynthesis genes at once. It changes the expression of phenylpropanoid enzymes *PAL* and *4CL*, the rate-limiting flavonoid enzyme *CHS*, and the flavonoid hydroxylase *CYP75B1*. The carbon flux is rerouted, but the whole network is stirred. It is impossible to tell whether the *CHS* gene alone does the job, or whether several genes must fire together. It gives correlation, not cause. Without isolating a single gene, the precise driver cannot be found.

The second limitation is endogenous feedback. In Chinese bayberry (*Morella rubra*), UV-B raises quercetin, but the plant fires its own brakes at the same time[2]. The transcription factor *MrBBX19* works with the core light-signaling factor *MrHY5* to activate the transcriptional repressor *MrNAC47*. This repressor simultaneously suppresses the transcriptional activator *MrMYB12* and the structural enzyme *MrF3H*. A second cascade involves *MrHY5* suppressing the microRNA *mru-miR396*, which allows another repressor, *MrGRF4*, to limit *MrMYB12*-dependent biosynthesis. The same signal that switches the pathway on also engages the endogenous brake. Native light regulation cannot bypass this built-in limit. It cannot reveal the true ceiling if the activator is opened while the brake remains active.

The third limitation is metabolic co-activation. In *Dendrobium officinale*, high-light treatment increases both anthocyanin and polysaccharide accumulation in the stems[3]. The mechanism reveals a shared switch. The transcription factor *DoHY5* directly activates the flavonoid enzyme *DoF3H1* and the polysaccharide enzymes *DoGMPP2* and *DoPMT28*. One light signal pulls multiple, distinct metabolic groups at once. It is practically impossible to boost the flavonoid fraction without dragging the polysaccharide fraction along. Native light regulation cannot wire these nodes independently. Because the native wiring is bundled, every species and every target must be decoded from zero.

Native light regulation tells us which nodes light can touch. It cannot isolate a single node for causal testing. It cannot bypass an endogenous brake. And it cannot combine multiple nodes into a programmable circuit. Answering these questions requires a tool that can pull a single gene out of the plant's own light network and control it independently.

4 The optogenetic toolbox

Native light regulation is a broadcast system. It cannot isolate one gene, bypass an endogenous brake, or wire several nodes together. Optogenetics is an addressable system. We assign a specific light channel to a specific gene.

4.1 From neurons to plant wiring

Optogenetics is most famous for its use in neuroscience. Its founding tools were *ChR2*, a blue-light-gated channel from green algae, and *NpHR*, a yellow-light chloride pump from an archaeon[5,6]. They share four engineering virtues. They are single components. They respond in milliseconds. They reverse when light leaves. And they stay silent in cells that never evolved them. These traits perfectly match the fast electrical logic of neurons.

These tools reveal a fundamental rule. The light-sensitive module must be exogenous. It cannot be the host's natural photoreceptor left in its native network. Only an exogenous module can be wired to a chosen target. If it stays native, light simply triggers the plant's ancient program. It does not become an independent switch. The switch must come from outside the existing system.

If the module must be exogenous, why not simply borrow *ChR2* from neuroscience? For plants, this physical logic does not work. Neurons transmit information through membrane voltages. Plants translate environmental signals into metabolic changes through transcription factors and promoters. Inserting an ion channel into a plant cell changes its membrane voltage, but it does not change gene expression. The signal language is entirely different (Fig. 1).

Plant optogenetics therefore requires exogenous light-controlled transcription modules. *PhyB-PIF* provides a red-light switch[7]. Its phytochrome B moiety originates from *Arabidopsis thaliana*, and its phytochrome-interacting factor (PIF) partner is a basic helix-loop-helix transcription factor from the same species. *CRY2-CIB1*, also from *Arabidopsis thaliana*, binds under blue light[8]. *CRY2* is a cryptochrome photoreceptor and *CIB1* is its interacting partner. *LOV2* is the light-oxygen-voltage (LOV) domain of phototropin 1 from oat (*Avena sativa*)[7]. Blue light causes its C-terminal helix to unfold, which can be coupled to enzyme activity or protein localization. The bacterial factor *EL222* comes from the marine bacterium *Erythrobacter litoralis*. It combines a LOV photosensor with a helix-turn-helix DNA-binding domain and acts as a blue-light-dependent transcriptional regulator. The cyanobacterial pair *CcaS-CcaR* originates from *Synechocystis* sp. PCC6803[9]. *CcaS* is a green-light-sensing histidine kinase and *CcaR* is its cognate response regulator. Together they drive gene expression from a specific promoter under green light.

4.2 How optogenetics closes the three gaps

The optogenetic toolbox provides three engineering solutions. Each solution addresses a core failure of native light regulation.

First, causal isolation. Under native light, such as UV-B, multiple genes are activated at once. When the target compound increases, the observer cannot tell which specific gene drove the change. One gene may act alone, or several may act together. This is correlation, not cause. Optogenetics solves this by changing one variable at a time. We take a single candidate gene, such as the rate-limiting enzyme for flavonoid synthesis, and wire it to an independent light switch. When the light is applied, only this gene is activated. The rest of the network remains silent. If activating this single gene is sufficient to increase the target compound, then the causal driver is isolated. However, a real experimental trap remains. If the test runs under normal white light, the plant's own photoreceptors will also activate the same gene. The native network and the engineered switch overlap, and the data become uninterpretable. The synthetic switch must therefore remain silent under white light. This leads directly to the second solution.

Second, input selectivity. Plants require broad white light for growth. White light naturally contains both red and blue components. It wakes almost every native photoreceptor. If the synthetic switch is also triggered by white light, the experiment is

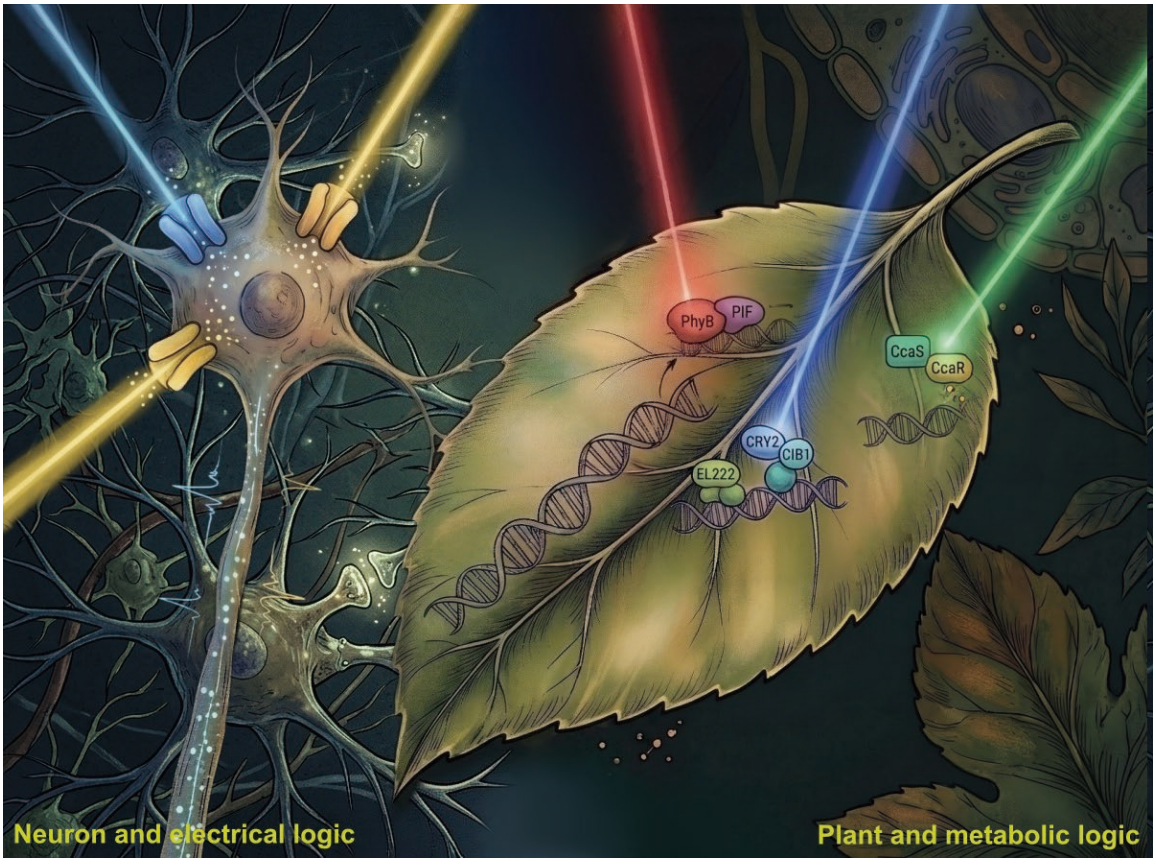

Figure 1 Divergent signal transduction logic in neurons and plants. Neurons rely on membrane voltage changes, while plants depend on transcription factor activation and gene expression.

contaminated. Optogenetic tools solve this by using orthogonal input channels. An orthogonal channel is a signal the plant does not already use.

Consider the plant usable light-switch elements (PULSE) system. It was developed in the model plant *Arabidopsis thaliana*. PULSE combines a red-light-inducible switch with a blue-light-regulated repressor[7]. Under white light, the blue component strongly activates the repressor, which overrides the red-light activation. The system is therefore held off. Only when the researcher applies pure red light, removing the blue component, does the repressor release the switch and gene expression begin. PULSE responds only to the specific red-light signal and stays silent under normal growth light.

Now consider the *CarH* system. It takes a chemical route to orthogonality. *CarH* is a bacterial transcription factor from *Thermus thermophilus* that requires a cofactor called AdoB12 to function[10]. Plant cells cannot synthesize AdoB12. Without externally supplied AdoB12, the switch remains inactive regardless of how much white light the plant receives. Only when the researcher adds AdoB12 and applies green light does *CarH* release its target promoter and allow gene expression. Because it depends on a cofactor the plant does not possess, the *CarH* switch is fully orthogonal to the plant's native light network even under white light.

One boundary must be stated. Orthogonality is selectivity at the input. It is not zero interference downstream. The metabolite produced by the switched gene can still feed back into the plant's network. The value of the switch is that the origin of the perturbation becomes identifiable. We know exactly where the intervention started.

Third, programmable combination. Native light often regulates multiple secondary metabolic pathways simultaneously. It bundles different pathways together. In *Dendrobium officinale*, for example, it drives anthocyanin and polysaccharide accumulation at the same time. The native network cannot separate them. Optogenetics allows different genes to be assigned different light switches. We can wire the anthocyanin-producing gene to a red-light switch and the polysaccharide-producing gene to a blue-light switch. Red light drives only the anthocyanin branch. Blue light drives only the polysaccharide branch. Multiple verified switches can coexist in one plant. By changing the light program, the same plant can output different compositional profiles. The bundle is broken. Control becomes programmable.

5 From causal proof to industrial translation

The industrial trouble with native light is now precise. A grower knows that changing the light spectrum changes the total chemical profile. The grower does not know which single genetic switch changes one target compound without disturbing the others. So growers hesitate to touch the spectrum. They fear that the target compound rises while yield falls. This is the trap of whole-plant control.

Causal validation provides the missing button. Suppose a single gene is wired to an independent light switch. Switching it raises a specific target compound while the plant grows normally. That gene is now a causal lever for that compound. It is no longer just a correlated marker. The moment that button is verified, three industrial applications emerge at once.

First, freedom from place and season. The switch is controlled by light, not by weather. Second, made-to-order chemistry. One branch can sit behind a green switch and another branch behind a purple switch. Green light gives a profile rich in one compound.

Purple light gives a profile rich in another. One facility, many recipes. Third, batch-to-batch consistency. A light program runs the same way every time in a controlled room. The ingredient profile becomes highly reproducible.

These three advantages replace the old industrial practice. Instead of blending many variable batches to achieve consistency, the industry can grow consistency into a single batch. Native light regulation tells us that the environment shapes the herb. Optogenetics tells us which gene precisely sets the potency. Together they let a factory tune a medicinal plant the way a chef tunes a recipe.

This vision is compelling, but the reality remains early. Short-term production will primarily rely on non-transgenic light treatments. Optogenetics remains a laboratory tool for mechanistic studies and causal validation, not a direct substitute for field production. Furthermore, the field must address whether introducing an exogenous light switch constitutes genetic modification, whether engineered medicinal plants require genetically modified organism labeling, and whether the market will accept such products.

Scientific bottlenecks also persist. Our understanding of synthetic-native interactions is limited, whole-plant orthogonality is difficult to maintain, and exogenous cofactor delivery is not yet practical. Future work should explore how light interacts with other environmental factors like temperature and water, and test the applicability of diverse optogenetic tools across different species. Therefore, a spike in a single target compound is not success. True success requires a reproducible chemical profile, acceptable biomass yield, and reliable post-harvest stability. This is the baseline for industrial translation.

6 Conclusion

While native light regulation cannot isolate a single gene, bypass endogenous brakes, or separate bundled pathways, optogenetics overcomes these barriers. It turns a broadcast signal into an addressable switch. The shift is not from natural to artificial. It is from uncontrolled to programmable.

The path forward requires rigorous causal testing and precise chemical profiling. But the direction is clear. "Grown" was a good first draft. "Programmed" is the next version. We are now writing the protocols to bridge them.

Data availability

Not applicable.

Conflicts of interest

The authors declare that there are no conflicts of interest in this work.

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Author contribution statement

Rui-Xuan Wang, Jing Li, Bao Yang, Yao-Guang Huang, Chen-Qi Niu and Qi-Wen Zhang: Writing–original draft. Xiu-Zhang Li: Conceptualization. Pei-Yan Ai: Writing–original draft and funding acquisition. Bai-Lin Li and Fen Liu: Conceptualization, writing–original draft. Cesarettin Alasalvar, Sui-Kiat Chang, Pu Liu and Hai-jiao Wang: Writing–review & editing.

Informed consent

Not applicable.

Ethics statement

Not applicable.

Use of AI statement

The images in this article feature original compositions; while some individual elements were generated by AI, the final images were drawn and refined by hand. The line drawings were uploaded to the Supplemental File for Review.

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