Trends in Biochemical Sciences

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Review

Multisensing photoreceptors: a cross-kingdom perspective

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Photoreceptors are classically depicted as monochromatic switches governed strictly by light. However, emerging biophysical and structural insights reveal that these proteins act as dynamic, multisensory hubs across kingdoms of life. Drawing primarily on plant and fungal systems, where mechanisms are most extensively characterized, this review synthesizes how photoreceptors integrate ambient temperature and cellular oxidative state alongside photon flux, with cross-kingdom examples extending this framework to bacteria. Thermal energy modulates dark reversion rates, quaternary assembly, and photobody phase separation, whereas reactive oxygen species alter the photocycle and trigger structural shifts through direct redox sensing. Under a 'stress-first' evolutionary model, ancestral stress-sensing scaffolds could be retrofitted with chromophores via exaptation, providing a unified biophysical rationale for how cells decode complex, fluctuating environments.

Highlights

Photoreceptors have classically been studied as pure light sensors, yet the natural settings they operate in couple light exposure to simultaneous shifts in temperature and oxidative state.

Whether a single receptor scaffold can reliably integrate such disparate inputs without sacrificing signaling specificity has remained a central open question in sensory biology.

Recent biophysical work has identified specific mechanisms, from phase separation and oligomeric switching to phosphorylation-mode transitions and direct redox sensing via conserved cysteines, by which photoreceptors read out temperature and oxidative state.

These findings indicate that multisensing is a widespread, inherent feature of photoreceptor scaffolds across kingdoms, potentially reflecting an ancestral property rather than a secondary elaboration.

Photoreceptors integrating light, temperature, and stress

The ability to monitor and adapt to fluctuating environmental conditions is a fundamental requirement for cellular survival. In natural ecosystems, light intensity, ambient temperature, and oxidative status are inseparably linked. High irradiance coincides with thermal stress and the production of **reactive oxygen species (ROS)** (see Glossary) through photosynthetic or metabolic pathways. Consequently, organisms that fail to integrate these cues risk cellular damage, such as protein misfolding or metabolic collapse [1–3]. This adaptive necessity has catalyzed a paradigm shift, moving away from isolated, linear signaling pathways toward a holistic model of signal integration [2,4]. A striking illustration of how deeply light and stress signaling are intertwined comes from the fungus *Aspergillus nidulans*, where **phytochrome**-dependent light signaling is transmitted not through a dedicated light-signaling cascade, but by directly co-opting the stress-activated mitogen-activated protein kinase (MAPK) SakA of the HOG pathway, which primarily responds to osmotic and oxidative stress [5]. In bacteria, a parallel case exists for *Bacillus subtilis*, where the blue-light receptor YtvA transmits its photosensory signal directly to the stressosome [6,7]. This convergence at the signal transduction level hints at a more general principle: light, temperature, and oxidative stress may not be perceived through separate sensory systems, but through shared molecular infrastructure. Building on this concept, recent biophysical studies have identified molecular mechanisms for temperature and ROS perception within these scaffolds, reshaping our understanding of sensory adaptation and the evolutionary origins of photoreceptor diversity [8,9]. This sensory versatility is rooted in a conserved modular architecture distributed across all kingdoms of life. Photoreceptors consist of a **photosensory module (PSM)** that contains a **chromophore**-binding pocket and is allosterically coupled to diverse **effector domains** that transduce environmental cues into physiological outputs, such as enzymatic activity, transcription factor recruitment, or nuclear translocation. This architectural modularity enables specialized spectral detection: **bilin**-binding canonical phytochromes employ reversible photoconversion to detect red and far-red light; retinal-binding opsins enable green-light perception; and flavin-based light–oxygen–voltage (**LOV**) proteins**,** blue-light using FAD (**BLUF**) proteins, and **cryptochromes (CRYs)** utilize covalent adduct formation to sense blue light (Figure 1) [11–13].

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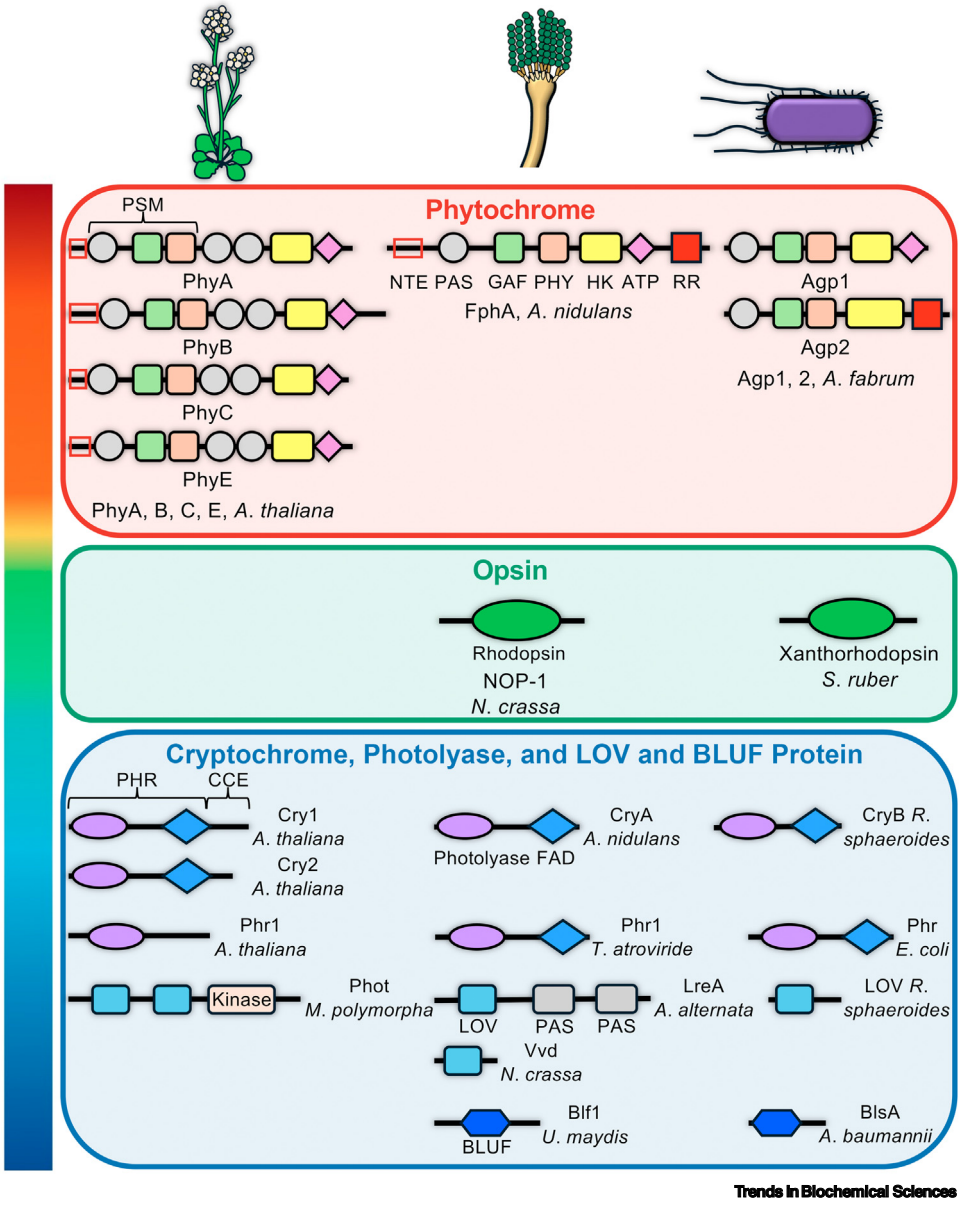


Figure 1. Predicted domain architecture of representative photoreceptors across plants, fungi, and bacteria. Photoreceptors are grouped by class (rows: phytochromes, opsins, and cryptochrome (CRY)/photolyase/LOV/BLUF proteins) and organism (columns: plants, fungi, and bacteria). The color bar (adapted from [10]) shows spectral range, from red/far-red (top) to blue (bottom). Phytochromes share a conserved PAS-GAF-PHY PSM paired with a C-terminal histidine kinase (HK, containing an ATP-binding site) domain. The N-terminal extension (NTE, highlighted by red boxes) is present in plant and fungal phytochromes, whereas the C-terminal response regulator (RR) is restricted to fungal and bacterial phytochromes. Opsins consist of a single rhodopsin domain without accessory domains and are absent in plants. CRYs, photolyases, and LOV- and BLUF-containing proteins display diverse modular architectures across the three domains of life. Plant CRYs (*A. thaliana* Cry1 and Cry2) feature an N-terminal photolyase homology region (PHR) coupled with a C-terminal extension (CCE), whereas plant photolyases (Phr1) and microbial orthologs (*A. nidulans* CryA, *Trichoderma atroviride* Phr1, *R. sphaeroides* CryB, and *Escherichia coli* Phr) consist primarily of the core PHR domain. LOV-domain proteins range in structural complexity from plant phototropins (*M. polymorpha* Mpphot) with tandem LOV domains and a C-terminal kinase domain, to fungal proteins with additional PAS domains (*A. alternata* LreA) or single, standalone LOV domains (*N. crassa* VIVID (Vvd) and *R. sphaeroides* LOV). BLUF-domain proteins are absent in plants but

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Glossary

Bilin: a linear tetrapyrrole and the chromophore of phytochromes. In canonical phytochromes, it undergoes reversible photoconversion between red- and far-red-absorbing states (Pr and Pfr).

BLUF: a blue-light-sensing, flavin-binding photoreceptor module found in some bacteria and fungi. It signals through hydrogen-bond rearrangement rather than covalent chromophore chemistry.

Chromophore: a light-absorbing cofactor embedded within a photoreceptor's sensory pocket (e.g., flavin, bilin, or retinal).

Conformational tuning: the concept that a photoreceptor's inherent structural flexibility allows nonphotic cues, such as temperature or redox state, to stabilize the same active conformations normally triggered by photon absorption.

Cryptochrome (CRY): a flavin-binding, blue-light photoreceptor structurally related to photolyases but lacking DNA-repair activity. It mediates photomorphogenic and circadian functions and, in some CRY2 variants, redox-signaling.

Effector domain: the domain of a photoreceptor, distinct from the PSM, that transduces signaling states into outputs such as enzymatic activity, transcription factor binding, or nuclear translocation.

Exaptation: an evolutionary process in which a protein scaffold or structural feature originally selected for one function (such as temperature or stress sensing) is co-opted for a new function, such as photoreception.

HOG pathway: a fungal 'high-osmolarity glycerol' MAP kinase cascade that coordinates osmotic and oxidative stress responses.

Intrinsically disordered region (IDR): a protein segment that lacks a defined three-dimensional structure when not interacting with other proteins.

Liquid–liquid phase separation (LLPS): the demixing of proteins into membraneless liquid condensates.

LOV domain: a 'light–oxygen–voltage' flavin-binding PSM found in plant, fungal, and bacterial blue-light receptors.

Molecular rheostat: a receptor whose signaling output scales continuously with combined input strength (e.g., photon flux and thermal energy), rather

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Despite their divergent chromophores and structures, these receptors rely on an inherent conformational flexibility to function. This flexibility implies that signaling states are not exclusively governed by photon absorption; instead, the protein scaffold's thermodynamics allow these receptors to integrate other environmental variables through '**conformational tuning**'. This architecture conforms to allosteric models, in which ligand- or stimulus-induced shifts between pre-existing conformational states, rather than the states themselves, determine functional output. In the LOV2-*Jα* system from *Avena sativa*, for example, photoactivation quantifiably shifts this conformational equilibrium toward the signaling-competent state [14]. Such biophysical adaptability enables photoreceptors to act as dual-purpose sensors that stabilize signaling-active states independently of light, thereby merging photoperception with temperature and ROS signaling to coordinate adaptive responses to environmental complexity.

This review examines how photoreceptors integrate temperature and oxidative stress alongside light detection, covering both the biophysical mechanisms of thermosensing and the mechanistic links between photochemistry and redox signaling. We focus primarily on phytochromes and the blue-light LOV, BLUF, and CRY proteins, whose dual-sensing mechanisms are the most mechanistically resolved to date. Opsins are discussed only briefly, as their nonphotic sensing capacity remains comparatively uncharacterized. We draw mainly on plant and fungal systems, where these mechanisms have been most extensively dissected, while incorporating bacterial examples to illustrate their broader evolutionary conservation.

Light and temperature

Temperature represents a dynamic environmental cue that is critical for survival due to its influence on molecular integrity, biochemical kinetics, and cellular architecture [15–18]. At the microscopic level, thermal energy accelerates Brownian molecular motion and disrupts noncovalent interactions that stabilize macromolecular structures. This kinetic influx drives transitions across diverse cellular components, such as fluidizing lipid bilayers to gate ion channels, melting RNA-thermometer hydrogen bonds to unmask ribosome-binding sites, or exposing hydrophobic regions in cytosolic chaperones [17–23]. Evaluating these systems requires distinguishing genuine thermosensitive elements, whose physical state is directly altered by thermal energy, from downstream effectors modulated by an upstream cascade. Emerging models position photoreceptors as dual-sensing integrators at this light–temperature interface, where photon flux and thermal energy directly converge on a shared conformational landscape via a flexible protein matrix.

The phytochrome system: integrating thermal cues through kinetic instability and phase separation

This thermodynamic integration is found in the phytochrome system, where recent biophysical and biochemical findings have redefined these 'spectral switches' as potent thermosensors. Temperature perception involves two primary, interconnected mechanisms: thermodynamic instability of their active states and the temperature-dependent stability of biomolecular interactions. While photon absorption drives activation from Pr (inactive red-absorbing state) to Pfr (active far-red-absorbing state), return to the Pr ground state can proceed via two distinct routes: light-driven photoconversion or **thermal reversion** (Figure 2, left). Kinetic modeling identifies this relaxation as a calibrated thermosensory mechanism [24–26]. In *Arabidopsis thaliana*,

than switching between discrete states, thereby enabling graded, tunable responses.

N-terminal extension (NTE): a regulatory segment preceding the PSM of plant and fungal phytochromes.

Output module (OPM): a C-terminal domain of phytochromes that drives self-association and downstream signal transduction.

Photobody (PB): a subnuclear, membraneless condensate formed by photoactivated phytochromes or Cry2 via LLPS.

Photolyase: a flavin-binding DNA-repair enzyme that uses light energy to reverse UV-induced lesions. It is evolutionarily related to CRYs within the CRY/photolyase family.

Photosensory module (PSM): the chromophore-binding core of a photoreceptor, allosterically coupled to its effector domain.

Phytochromes bilin-binding photoreceptors. Canonical phytochromes interconvert between an inactive, red-absorbing (Pr) and an active, far-red-absorbing (Pfr) state.:

Reactive oxygen species (ROS): chemically reactive oxygen-derived molecules, including superoxide, hydrogen peroxide, singlet oxygen, and hydroxyl radical, that are generated as an obligatory byproduct of chromophore photochemistry.

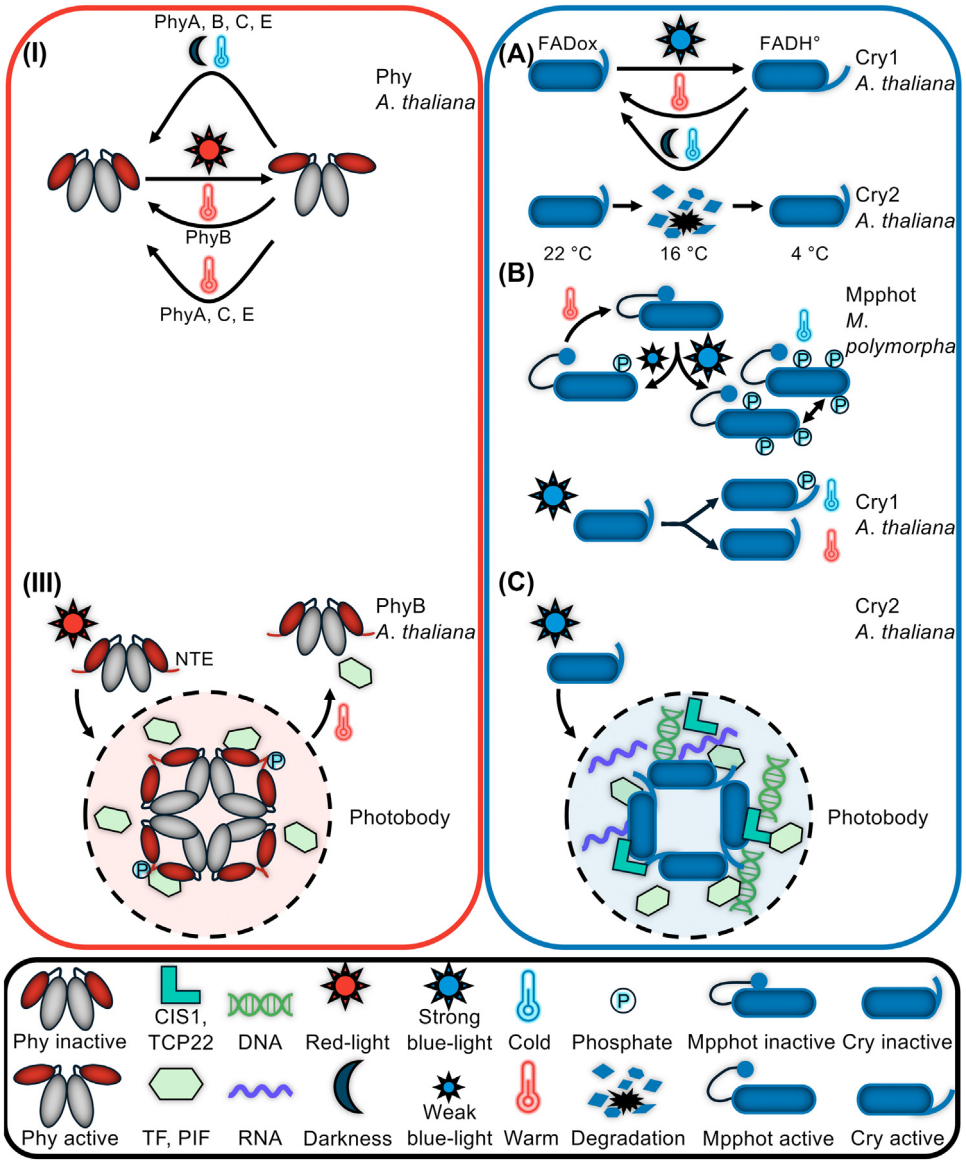
ROS-wave: the rapid, systemic propagation of a reactive-oxygen-species signal between cells, coordinating whole-plant responses such as stomatal closure after local stress exposure.

Thermal reversion: the temperature-dependent, light-independent return of a photoreceptor from its active to its inactive state.

Thermomorphogenesis: temperature-driven developmental adaptation in plants, controlled largely by light- and temperature-dependent inactivation of PhyB.

White-collar complex (WCC): a fungal blue-light photoreceptor complex (White-collar 1/White-collar 2) that acts as a light-activated transcription factor and a hub for redox-balancing gene programs.

function as standalone single-domain photoreceptors in fungi (*Ustilago maydis* Blf1) and bacteria (*A. baumannii* BlsA). Domain boundaries are schematic; sizes are not to scale. Agp: *Agrobactrium* phytochrome; Blf1: BLUF-domain protein 1; BlsA: blue-light-sensing A; BLUF: blue-light using flavin; CRY: cryptochrome; FAD: flavin adenine dinucleotide; FphA: fungal phytochrome A; GAF: cGMP-specific phosphodiesterases/adenylyl cyclases/FhI domain; LOV: light–oxygen–voltage; LreA: light-response A; NOP-1: Neurospora opsin 1; PAS: per-arnt-sim; Phot: phototropin; Phr: photolyase; PHR: phtolyase homology region; Phy: phytochrome; PHY: pyhtochrome-specific domain; PSM: photosensory module; Vvd: VIVID.



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Figure 2. Shared and receptor-specific kinetic principles of thermosensing in phytochromes versus cryptochromes/LOV proteins. (I/A) Reversion kinetics and proteostasis dictate thermosensory readouts across receptor classes. Left: red/far-red photoconversion of Pr to Pfr is reversed by temperature-dependent dark reversion; PhyB exhibits fast, temperature-tuned kinetics that track diurnal temperature cycles, whereas PhyA, PhyC, and PhyE revert far more slowly and function as dedicated photon counters. Right: In the blue-light receptor Cry1, low temperatures kinetically delay the reoxidation of the FAD chromophore. Additionally, Cry2 exhibits distinct proteostatic tuning, being targeted for degradation at moderate temperatures (16°C), while remaining stabilized at chilling temperatures (4°C). (B) Light- and temperature-dependent phosphorylation mechanisms in blue-light receptors: Thermal reversion regulates the balance between monomeric states favoring cis-autophosphorylation (at standard growth temperatures) and active receptor accumulation driving intermolecular assembly for trans-autophosphorylation in *M. polymorpha* phototropin (Mpphot). In parallel, blue-light-induced phosphorylation of Cry1 is repressed at elevated temperatures. (III/C) Convergence on nuclear condensate formation (photobodies, PBs): PhyB (via its NTE) forms temperature-sensitive PBs with phytochrome-interacting factors (PIFs) and DNA that undergo dissolution at high temperatures. Cry2 forms blue-light-induced PBs with transcription factors (TFs), CIS1, TCP22, DNA, and RNA, enhancing CIS1 recruitment under cool ambient temperatures. Cry2 and PhyB colocalize in shared subnuclear hubs to integrate light and temperature inputs.

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phytochrome B (PhyB), a major plant photoreceptor important for growth and development, integrates cues through its temperature-dependent Pfr-reversion. Under illumination, the active Pfr pool reflects the balance between light-driven activation and thermal decay. Rising temperatures shift this equilibrium toward the inactive Pr state, triggering **thermomorphogenesis** [27–29]. Kinetic analysis reveals a functional divergence: PhyB's tuned reversion tracks diurnal temperature cycles as a primary thermosensor, while isoforms with significantly slower thermal reversion kinetics (PhyA, PhyC, and PhyE) function as dedicated photon counters, a divergence observed across *Arabidopsis* and other plant species (Figure 2, left) [29]. Although the **N-terminal extension (NTE)** and its **intrinsically disordered region (IDR)** influence these kinetics, they do not explain PhyB's uniquely fast thermal reversion. This points to the PSM as the responsible domain, though no specific amino acid or motif therein has been identified to date [28–30]. This thermosensory logic extends beyond plants, as comparable thermal reversion kinetics also govern the bacterial phytochrome Agp2 from *Agrobacterium fabrum* [25,31] and the fungal phytochrome FphA in *A. nidulans*, underscoring conservation across kingdoms [26].

Complementing these kinetic properties, PhyB in *A. thaliana* integrates light and temperature signals at the mesoscale through **liquid–liquid phase separation (LLPS)**. Photoactivated PhyB forms subnuclear **photobodies (PBs)**, membraneless condensates that serve as tunable thermosensory hubs [32,33]. PB biogenesis relies on modular cooperation: the C-terminal **output module (OPM)** acts as a self-associating domain, driving oligomerization, while the NTE functions as a phase-separating IDR stabilizing the assembly, a role that later intersects with PIF-mediated signaling (Figure 2, left) [32,33]. Notably, PIF binding is not required for PB formation itself. This modular cooperation positions the NTE as the biophysical interface translating kinetic signals from the PSM into spatial phase transitions. Intriguingly, while the NTE is not the primary factor for thermal reversion, it is essential for PhyB's thermosensing capacity, modulating phase behavior to trigger PB dissolution at high temperatures. This is strictly sequence-dependent: NTE deletion abolishes the thermoresponsiveness of PhyB condensates, a property no other IDR can restore [33]. Specific NTE amino acids respond to temperature by adjusting their adhesive interactions, directly modifying condensate behavior and solubility. NTE phosphorylation further tunes both dark reversion and PB temperature-dependent behavior [33]. Physiologically, assembled PBs recruit and sequester phytochrome-interacting factors (PIFs), facilitating their degradation. Heat-induced PB dissolution releases these factors, attenuating PhyB-mediated inhibition and promoting growth-related gene expression (Figure 2, left) [32,33].

Together, these findings indicate that temperature-tuned photocycle kinetics represent a conserved core of phytochrome thermosensing across plants, fungi, and bacteria, onto which plants have added a further layer of NTE-dependent phase separation into PBs. This additional layer turns the shared timing signal into precise control of gene expression.

The blue-light system: kinetic diversity and hierarchical thermosensing architecture

Blue-light receptors enable temperature sensing through diverse mechanisms that reflect their structural heterogeneity. While the phytochrome system serves as a centralized thermostat for growth, blue-light receptors appear tuned to specific thermal windows, from cold-avoidance to seasonal acclimation. Paralleling red-light sensors, the signaling state in blue-light systems is

CIS1: Cry2-interacting splicing factor 1; Cry: cryptochrome; FAD: flavin adenine dinucleotide; FADH: FAD reduced (semiquinone); FADox: FAD oxidized; LOV: light–oxygen–voltage; Mpphot: *Marchantia polymorpha* phototropine; NTE: N-terminal extension; Pfr: phytochrome far-red; Phy: phytochrome; Pr: phytochrome red; TCP22: teosinte branched/cyclo-idea/proliferating cell factor 22.

fundamentally governed by temperature-dependent kinetics, as shown for plant CRYs and phototropins (Figure 2, right) [34,35], as well as bacterial LOV proteins [36]. In YtvA from *B. subtilis*, dark-recovery kinetics are temperature-dependent and differ between the full-length protein and its isolated **LOV domain** [36].

Besides the influence on reversion kinetics, temperature-dependent effects include changes in quaternary structure. Structural studies on the isolated LOV receptor from the bacterium *Rhodobacter sphaeroides* illustrate that temperature and light act synergistically to control dimerization. Since many LOV domains exist in a temperature-dependent monomer–dimer equilibrium, a rising temperature shifts this equilibrium toward the dissociated, monomeric state. By integrating these cues, the receptor functions as a **molecular rheostat**, in which the physiological output is a product of both photon flux and the kinetic energy of the system, enabling precise tuning to the microclimate [37]. In the liver moss *Marchantia polymorpha*, this biophysical principle is exemplified by the phototropin Mpphot, which utilizes the thermal reversion of its LOV domains to monitor absolute temperature [38]. At standard growth temperatures, rapid thermal reversion limits Mpphot to cis-autophosphorylation. Low temperatures decelerate reversion, and cumulative cis-autophosphorylation is proposed to trigger a structural switch enabling trans-autophosphorylation between adjacent molecules (Figure 2, right), acting as a digital logic gate. Here, the convergence of low thermal energy and high light intensity produces a hyperphosphorylated state, a signal for the cold-avoidance response. Whether this reflects temperature-dependent dimerization or a phosphorylation-driven structural change remains unresolved [38,39].

While LOV-based receptors, like phototropins, primarily leverage kinetic shifts in their quaternary assembly, CRYs integrate thermal information through a more stratified, hierarchical framework. This involves a combination of chromophore kinetics, proteostatic shifts, and mesoscale organization. At the fundamental molecular level, blue-light signaling is sustained under low temperature because reoxidation of the flavin adenine dinucleotide (FAD) chromophore slows kinetically (Figure 2, right) [34]. This kinetic sensitivity is further amplified by unique proteostatic responses in Cry2 from *A. thaliana*. While the protein is degraded under moderate temperatures (16°C), it is stabilized at chilling temperatures (4°C) (Figure 2, right), where it protects the transcription factor ELONGATED HYPOCOTYL 5 (HY5) from degradation mediated by the E3 ubiquitin ligase CONSTITUTIVELY PHOTOMORPHOGENIC 1(COP1), enabling cold acclimation [40–42]. In parallel, blue light also induces Cry2 to form PBs via LLPS [43,44] (Figure 2, right). Similar to PhyB, this process is driven by its photolyase homology region and an intrinsically disordered CRY C-terminal extension (CCE) [44]. These PBs serve as signaling platforms that recruit diverse partners, such as the transcription factor TCP22, which regulates the circadian clock, and the RNA-binding protein CIS1 [45]. During thermal adaptation, cool ambient temperatures enhance Cry2 recruitment to CIS1, an association that modulates the alternative splicing of *FLOWERING LOCUS M*, allowing the plant to tune its reproductive timing to ambient chill [32,45,46]. While Cry2 predominantly governs responses to chilling, Cry1 extends the sensory range to elevated temperatures. Heat-induced repression of its phosphorylation suggests a distinct mode of temperature perception (Figure 2, right). This enzymatic tuning impacts the Cry1–Cop1–Hy5 axis [47] and promotes heat shock gene expression through the heat-shock transcription factor HSFA1d [48], demonstrating that blue-light-induced condensates also function as critical platforms for heat stress adaptation [32]. However, unlike PhyB, where temperature sensitivity is intrinsically encoded in the NTE, it remains unclear to what extent the formation and stability of CRY PBs are directly governed by temperature. Ultimately, Cry2 and PhyB interact and colocalize in PBs, creating integrated 'signaling hubs' that allow the plant to function as a sophisticated sensory integrator. By recruiting interaction partners, these hubs dynamically tune their composition and stability to the combined inputs of ambient light and heat [32,33,43].

Together, these findings show that, as in phytochromes, temperature-tuned photocycle kinetics form a conserved core of blue-light thermosensing across bacteria and plants. Blue-light receptors additionally layer on proteostasis- and phosphorylation-based readouts, ultimately converging with phytochrome signaling in shared PBs.

Light-independent perception: thermodynamic flexibility and molecular mimicry

The emergence of these integrated signaling hubs suggests that dual sensing is a central feature of the light-response machinery. However, this raises the fundamental question of whether such thermosensory capacity strictly depends on photoactivation or represents an intrinsic protein property that can operate in total darkness. Such a phenomenon has been described in bacteria and fungi, where certain photoreceptors appear to function as light-independent thermometers [8,37,49].

The molecular basis for light-independent perception lies in the inherent thermodynamic flexibility of photoreceptor proteins, which exhibit conformational dynamics in darkness that mimic light-activated states. This thermal mimicry is exemplified by the LOV module from the Gram-negative bacterium *R. sphaeroides*, where ambient heat triggers the linear unfolding of key structural elements, specifically *the Jα* and *Kα* flanking helices, mimicking the structural state triggered by light absorption [37]. While structurally distinct, the BLUF-type receptor blue-light-sensing A (BlsA) from another Gram-negative bacterium, *Acinetobacter baumannii*, reveals an FAD-binding site uniquely sensitive to temperature-induced structural changes (Figure 3). These structural alterations influence photoactivation and could further induce temperature-dependent shifts in the protein oligomerization state, acting as a regulatory switch that tunes binding affinities to trigger specific physiological responses [49]. The functional link between photochemical capacity and thermosensing is highlighted by the C421S mutant of the LOV-domain blue-light receptor light response A (LreA) in the fungus *Alternaria alternata*. Although the LOV domain retains its scaffold integrity, allowing the noncovalent incorporation of the chromophore within the binding pocket, the substitution of this cysteine (Cys) residue, essential for photochemical adduct formation, abolishes thermal responsiveness (Figure 3) [8]. Similarly, the fungal phytochrome FphA from *A. nidulans* exhibits spectral properties that resemble those of free biliverdin under elevated temperatures, suggesting a softening of the chromophore-binding pocket (Figure 3) [26].

Building upon such localized structural fluctuations, receptors employ structural extensions or catalytic domains that serve as biochemical thermometers. The NTE, exclusive to fungal and plant phytochromes, modulates PB stability through thermal sensing in *Arabidopsis* [33]. A comparable NTE in the fungal phytochrome FphA stabilizes its active Pfr state, indicating that IDR-based modifiers are not restricted to plants [50]. Temperature perception is also encoded in enzymatic activity: Cry1 phosphorylation in *A. thaliana* is heat sensitive [47], and in *A. nidulans*, temperature-dependent phosphorylation of YpdA downstream of FphA reflects thermal modulation of phytochrome histidine kinase signaling (Figure 3) [26]. A comparable temperature dependence governs the bacterial phytochrome Agp1 from *A. fabrum*, whose histidine kinase activity is reversibly suppressed above 35°C. Prolonged irradiation at these temperatures also drives Pfr into a distinct third spectral state, a light- and temperature-dependent transition that requires the kinase module itself [31,51].

These findings indicate that light and temperature perception converge on a shared mechanism at the chromophore-binding pocket, utilizing the same molecular trigger to shift the receptor into an activated state. Beyond the pocket itself, accessory structural and catalytic modules extend this sensory interface further. Such conservation across disparate folds and organisms reflects convergent biophysical evolution.

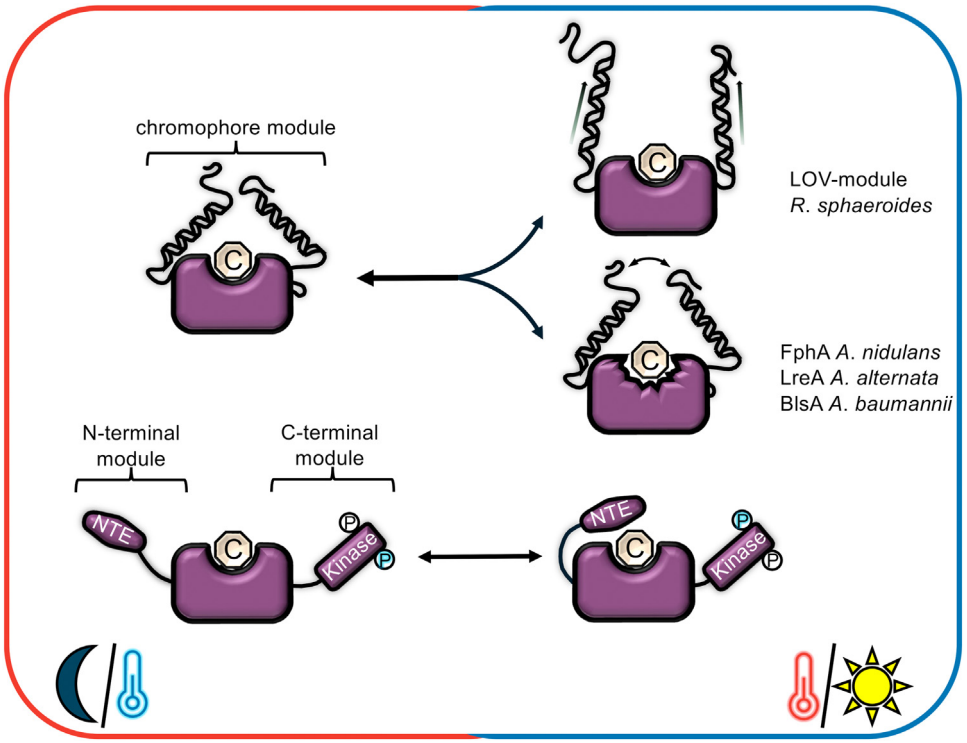


Figure 3. Proposed models for light-independent thermosensing in photoreceptors. Temperature perception can be mediated either through the core chromophore module or through regulatory structural extensions. Top: the chromophore module is intrinsically temperature-sensitive. Elevated temperature unfolds the flanking *Jα/Kα* helices in the LOV-module of *R. sphaeroides* or influences the chromophore-binding pocket in the phytochrome FphA (*A. nidulans*), the LOV-domain receptor LreA (*A. alternata*), and the BLUF protein BlsA (*A. baumannii*); both changes mimic the light-activated conformation. Bottom: alternatively, thermosensitivity is driven by flanking domains. Thermal shifts either induce conformational changes in the N-terminal extension (NTE) or alter the C-terminal output domain, such as the kinase domain's phosphorylation pattern, thereby regulating downstream signaling. The icons at the bottom left and right represent the two conditions modeled: darkness or cold temperature (moon, blue thermometer) versus light or warm temperature (sun, red thermometer). BlsA: blue-light-sensing A; BLUF: blue-light using FAD; LreA: light-response A; FphA: fungal phytochrome A; LOV: light–oxygen–voltage.

Light and stress

The principle of integrated environmental sensing extends naturally beyond the temperature axis, as irradiance drives the chemistry that gives rise to oxidative, osmotic, and related cellular pressures. Flavin cofactors in LOV and CRY scaffolds are redox-active chromophores whose photoexcited states transfer electrons to molecular oxygen [52]. Bilin chromophores engage this route less efficiently [53], suggesting that their contribution to redox signaling may rely on chromophore-independent mechanisms [54]. The result is the continuous production of ROS, including superoxide ($O_2^{\bullet -}$), hydrogen peroxide (H_2O_2), singlet oxygen ($^1O2$), and hydroxyl radicals [55,56]. Intervals of high irradiance also coincide with desiccation, ionic imbalance, and the osmotic perturbations that follow water loss; in pathogenic and symbiotic interactions, light intensity additionally becomes a proxy for surface exposure and host immune ROS-burst attack [57,58].

From this perspective, the evolutionary recruitment of photoreceptors as stress sensors is parsimonious rather than coincidental. A single redox-active chromophore embedded in a conformationally flexible scaffold can simultaneously report photon flux and the chemical state of its immediate environment; relaying both signals through a shared OPM avoids maintaining

parallel sensory machinery. Three logical consequences follow. First, the architectural principles that enable thermal tuning can also allow for redox-dependent and osmotically dependent conformations. Second, because the photocycle itself generates ROS as an obligatory byproduct of flavin or biliverdin reoxidation, photoreceptors are intrinsically equipped to encode the oxidative state in their own activity cycles [8,59–61]. Third, photoreceptor signaling outputs frequently converge on the same transcriptional hubs found in most organisms and governing antioxidant biosynthesis, osmolyte production, and DNA repair [62,63]. This convergence allows light activation to preemptively remodel the cellular stress transcriptome before damage accumulates.

Cryptochromes and photolyases: a redox sensor built into the photocycle itself

The CRY/**photolyase** family unites the dual-sensor concept in its most explicit form. The flavin photocycle necessarily produces ROS during reoxidation, so light activation is biochemically inseparable from a transient oxidative event [61]. *Arabidopsis* Cry1 and Cry2 exploit this directly: blue-light activation drives the nuclear accumulation of H_2O_2 and ROS. This induces a panel of biotic- and abiotic-stress-responsive transcripts, including antioxidant and pathogen-defense genes, and, crucially, continues to do so when canonical photomorphogenic signaling is genetically disabled. This mechanism defines CRY-driven nuclear ROS biosynthesis as a parallel signaling axis [59]. CRYs can also engage ROS as ligands rather than mere byproducts: simulations of avian or plant CRYs reveal that superoxide transiently binds within the 'crypt' region adjacent to the FAD pocket, providing a structural basis for direct redox sensing (Figure 4, middle) [55,64,65]. Beyond redox sensing, recent work shows that *Arabidopsis* Cry2 is required for chloroplast-generated singlet-oxygen signaling and programmed cell death, a role preserved in Cry2 variants lacking canonical blue-light signaling, establishing a light-independent function for this 'light' receptor in retrograde photo-oxidative-stress acclimation [66].

The same principle operates where the photic stimulus is absent: blind cavefish retain a functional CPD photolyase that repairs oxidatively modified bases, such as 8-oxo-2'-deoxyguanosine, in the dark, showing that the photolyase fold itself can function as a redox-targeted enzyme [67]. The conservation of light/ROS crosstalk extends to vertebrate cis-regulatory elements: the D-box enhancer mediating light-induced clock gene expression in zebrafish is a direct nuclear ROS target, indicating that light and oxidative inputs converge at the promoter level [68].

In fungi, this dual-sensor logic is exemplified by *A. nidulans*, where the photolyase-like CryA relocates from the nucleus to mitochondria via a redox-sensitive N-terminal Cys (Figure 4, bottom). In the nucleus, CryA establishes negative-feedback loops with the phytochrome FphA and the **HOG-pathway** activating transcription factor A (AtfA). This reveals CryA as a central integrator of light and oxidative stress [9]. The same architecture appears to be conserved in distantly related Sordariomycetes and bacteria. Here, CRY/photolyase family (CPF) proteins control the sensitivity to osmotic and oxidative stress and promote survival, growth, and intracellular redox homeostasis [69,70]. Fungal opsins extend this pattern: Neurospora opsin 1 (NOP-1) deletion in *Neurospora crassa* reshapes the expression of oxidative-stress-response and proton-transport proteins [71].

Across plants, animals, fungi, and bacteria, the CPF couples photon perception to intracellular ROS signaling and in several lineages also functions as a direct redox-state sensor. This recurrence across phylogenetically distant systems indicates that light and oxidative-input integration is an evolutionarily conserved property of the CPF fold, not a series of independent adaptations.

The light–oxygen–voltage and phytochrome systems: redox sensors and upstream switches for stress programs

The LOV scaffold has long been considered a candidate light-redox interface, since its cofactor is a redox-active flavin whose photochemistry depends on a single conserved Cys [72]. Several

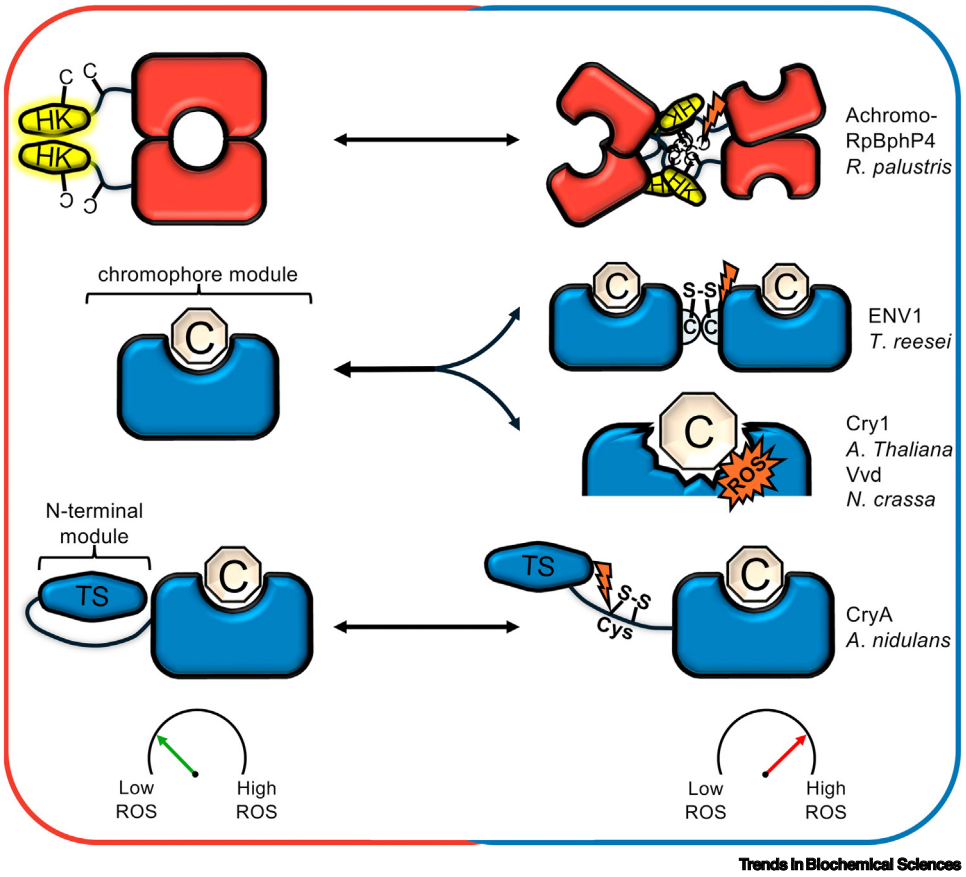


Figure 4. Proposed models for redox-based perception of oxidative stress in photoreceptors. The model is based on the chromophore-module/accessory-domain logic of Figure 3. Top: redox state can toggle quaternary structure itself: in achromo-RpBphP4 (R. palustris), reducing conditions favor a histidine kinase (HK)-active homodimer, while oxidizing conditions Cys-mediated disulfide crosslinking into a higher-order, kinase-inactive aggregate. Middle: the chromophore-binding pocket itself serves as a site for ROS sensing via distinct mechanisms: oxidation of paired cysteines to an intermolecular disulfide drives homodimerization in ENVOY (*T. reesei*); Cry1 (*A. thaliana*) binds superoxide as a ligand within its 'crypt' pocket; and VIVID (*N. crassa*) accumulates light-induced oxidative damage in its flavin pocket. The orange flash symbol represents these ROS-induced structural modifications. Bottom: a reversible disulfide bond toggles a targeting sequence (TS), such as the mitochondrial targeting signal of CryA (*A. nidulans*), between masked (low-ROS) and exposed (high-ROS) states, thereby determining its subcellular localization. The icons at the bottom left and right indicate the two modeled redox conditions: low ROS versus high ROS. CRY: cryptochrome; Cys: cysteine; ENV1: ENVOY1; ROS: reactive oxygen species; RpBphP4: *Rhodopseudomonas palustris* bacteriophytochrome P4; S-S: disulfide bond; VIVID: *Neurospora crassa* blue-light receptor; Vvd: VIVID.

cases support a dual-sensor reading: ENVOY from the fungus *Trichoderma reesei* carries an evolutionarily repositioned active-site Cys that integrates blue-light and redox inputs. Under oxidative stress, ENVOY sequesters as a homodimer, blocking its heterodimerization with BLR1 (Figure 4, middle) [73,74]; the Cys-less, LOV-like protein of the bacterium *Magnetospirillum magneticum* retains H_2O_2- and morphogenesis-related outputs even without canonical photochemistry [75], consistent with evidence that LOV receptors lacking the adduct-forming Cys can still support light-driven signal transduction [76]. A parallel case exists among bacteriophytochromes, where loss of the bilin chromophore in some *Rhodopseudomonas palustris* strains repurposes the same photosensory scaffold as a dedicated redox sensor. Redox-active cysteines in its phytochrome (PHY) and kinase domains mediate this: reducing conditions favor a kinase-active homodimer, while oxidation drives disulfide-linked aggregation

that silences kinase activity (Figure 4, top) [54]. In the fungus *N. crassa*, VIVID accumulates light-induced oxidative damage in its flavin pocket (Figure 4, middle), consistent with singlet-oxygen generation via Dexter energy transfer from the flavin triplet state rather than through flavin oxidation or reoxidation, and behaves transiently as a photosensitizer [77].

Bacterial LOV proteins extend this to prokaryotes: in *Brucella*, a LOV-histidine kinase activates the general-stress regulon, and in *Rhodobacter* species, LOV sensors feed into σ-factor cascades and singlet-oxygen-responsive regulators [57,78]. In plants, phototropin(res govern chloroplast movement, stomatal aperture, and photoprotective genes against photooxidative damage [79]. Meanwhile, *Arabidopsis* PhyB drives the NADPH-oxidase **'ROS-wave'** coordinating high-light stomatal closure, while its downstream module (PIFs at ROS-responsive promoters, HY5/HYH at redox-enzyme genes) reshapes the antioxidant and salt-acclimation transcriptome [62,80–82]. The same logic is conserved in fungi, where *A. nidulans* phytochrome feeds into the SakA/HOG MAPK cassette, providing the substrate for CryA-mediated oxidative-stress circuits [9,83].

Together, these cases point to two modes: redox-active cysteines or chromophore photochemistry can make LOV and phytochrome scaffolds direct redox sensors, whereas in systems such as the **white-collar complex (WCC)** of *Fusarium asiaticum* and *Botrytis cinerea*, light remains the primary cue, and loss of a WCC component compromises redox-balancing programs downstream of blue-light input [84,85].

Concluding remarks

The paradigm of photoreceptors operating as simple, monochromatic light switches has evolved into a more dynamic framework. Light perception appears to be intertwined with thermal and oxidative sensing across all kingdoms of life. From fungal stress–MAPK modules [5] to plant PB dynamics [32,33], nature leverages the inherent biophysical flexibility of photoreceptor scaffolds to integrate multiple environmental inputs into a unified cellular output.

From an evolutionary standpoint, the widespread occurrence of multisensing photoreceptors across distant clades raises a fundamental question: did thermosensing and redox responsiveness evolve as secondary adaptations, or are they ancestral features of photosensory scaffolds? We propose that the ecological and evolutionary timeline strongly favors a 'stress-first' model (Figure 5). Early unicellular organisms inhabiting aphotic primordial environments were constantly exposed to thermal fluctuations and metabolic ROS long before light became relevant for survival. Under this framework, ancestral photoreceptor scaffolds initially evolved not as light sensors, but as stress monitors long before photodynamic chromophore integration occurred. The subsequent recruitment of light-absorbing chromophores into pre-existing stress-responsive scaffolds during the colonization of illuminated niches represents a classic process of **exaptation**, grafting photoperception onto an already dynamic matrix [86]. A similar logic may extend to other metalloenzymes: nitrogenase itself may have initially lacked its molybdenum cofactor entirely [87] or relied on simpler iron-sulfur cluster precursors that only later matured into the elaborate iron-molybdenum cofactor (FeMoCo) within the same conserved protein scaffold [88]. This evolutionary trajectory provides a unified rationale for why chromophore-binding pockets across diverse receptor families remain flexible, modular, and susceptible to nonphotic inputs today. Because the chromophore pocket was retrofitted into an inherently flexible stress sensor, thermal kinetic energy and ROS-driven modifications continue to directly perturb the conformational landscape surrounding the chromophore. This concept explains why temperature-dependent dark reversion and structural tuning remain universal features of phytochromes, LOV domains, BLUF proteins, and CRYs. Which readout predominates, however, likely depends on protein-specific accessory domains, such as kinases, NTEs, or CCEs, appended to the pocket (Figure 5). Rather than being evolutionary 'noise'

Outstanding questions

Evolutionary origins: does redox and temperature sensing by photoreceptors reflect an ancestral, 'stress-first' function present in early apo-proteins, or is it a convergent, lineage-specific co-option of shared chromophore chemistry?

Pathway specificity and crosstalk: how do photoreceptors interface with general stress modules (such as the fungal SakA/HOG MAPK pathway) to transmit photic signals without losing signal specificity between light and abiotic stress?

Uncoupling functions: can specific amino acid substitutions be identified that separably uncouple photochemistry from temperature or redox sensing, clarifying whether these properties are mechanistically inseparable or independently tunable?

Cross-kingdom phase separation: do fungal or animal photoreceptors possess NTE-like intrinsically disordered modules that confer temperature-dependent phase separation, analogous to plant phytochromes?

Photochemical versus direct redox sensing: to what extent do photoreceptors rely on ROS generated as obligatory byproducts of chromophore photochemistry, compared to directly sensing the cellular redox state through conserved redox-active residues?

Redox-driven shuttling: through what precise structural shifts do ROS-driven modifications (such as disulfide bonding) trigger subcellular relocalization, as seen in the nuclear-to-mitochondrial shuttling of fungal cryptochromes?

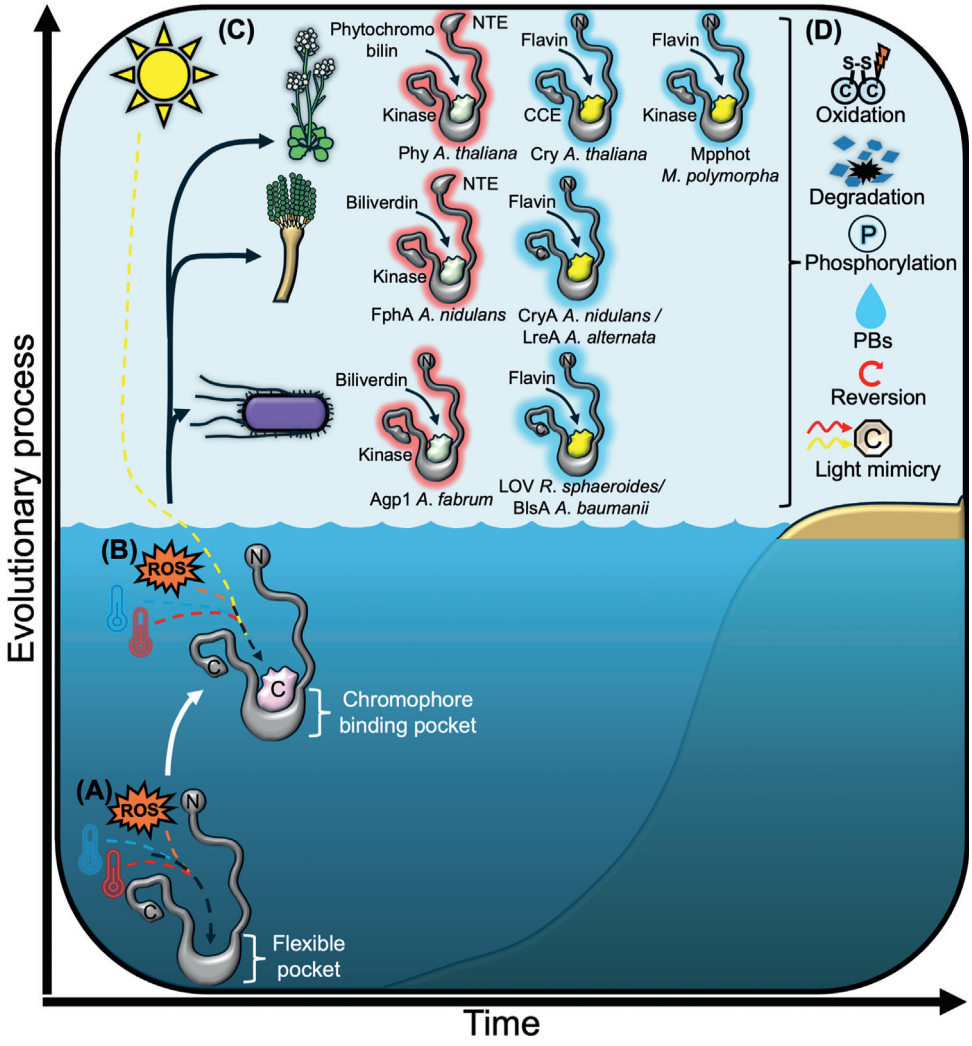


Figure 5. A stress-first model for the evolutionary origin of photoreceptor diversity. (A) An ancestral, prephotic protein already possesses a flexible ligand-binding pocket and responds intrinsically to thermal energy and reactive oxygen species (ROS) without a chromophore. (B) Exaptation: through evolution, the same flexible pocket is retrofitted with a light-absorbing chromophore (C), converting the ancestral stress sensor into a photoreceptor while retaining its underlying sensitivity to temperature and ROS. (C) Following chromophore integration, structurally distinct photoreceptor families diversified in parallel across plants, fungi, and bacteria, each pairing a specific chromophore, phytochromobilin, biliverdin, or flavin, with accessory domains (N-terminal extension, NTE; C-terminal cryptochrome extension, CCE; and histidine kinase, HK) that couple photoperception to nonphotic outputs. Representative examples: Phy and Cry from *A. thaliana*; Mpphot from *M. polymorpha*; FphA and CryA from *A. nidulans*; LreA from *A. alternata*; Agp1 from *A. fabrum*; LOV from *R. sphaeroides*; BlsA from *A. baumannii*. (D) The accessory domains and chromophore chemistry in (C) support distinct nonphotic signaling readouts: Cys oxidation, proteostatic degradation, phosphorylation, phase separation into photobodies, thermal reversion, and light-state mimicry. Agp1: *Agrobacterium* phytochrome 1; BlsA: blue-light sensing A; CryA: cryptochrome A; Cys: cysteine; FphA: fungal phytochrome A; LOV: light–oxygen–voltage; LreA: light-response A; Mpphot: *Marchantia polymorpha* phototropine; PBs: photobodies.

or unintended side effects, thermal sensitivity and redox responsiveness could reflect the ancestral foundation upon which photoperception was built. We do not consider this foundation limited to temperature and redox state: environmental pH is emerging as a further, potentially nonphotic stimulus, with recent evidence that pH directly modulates bacterial phytochrome photoreception [89].

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Testing this model will require ancestral sequence reconstruction and comparative analysis of stress-responsive apo-scaffolds, alongside deciphering how photoreceptors uncouple photochemistry from nonphotic inputs, maintain pathway specificity within stress networks, and exploit redox-driven shuttling and phase separation across kingdoms (see Outstanding questions). Unraveling these mechanisms will deepen our understanding of ecological adaptation and illuminate fundamental principles of protein folding, allosteric signal propagation, and the evolutionary mechanics that allow a single protein chassis to decode environmental complexity.

Declaration of interests

The authors declare no competing interests.

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