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Shining a light on the Arabidopsis circadian clock

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Abstract:	<p>The circadian clock provides essential timing information to ensure optimal growth to prevailing external environmental conditions. A major time-setting mechanism (zeitgeber) in clock synchronisation is light. Differing light wavelengths, intensities and photoperiodic duration are processed for the clock-setting mechanism. Many studies on light-input pathways to the clock have focused on <i>Arabidopsis thaliana</i>. Photoreceptors are specific chromic proteins that detect light signals and transmit this information to the central circadian oscillator through a number of different signalling mechanisms. The most well characterised clock-mediating photoreceptors are cryptochromes and phytochromes, detecting blue, red and far-red wavelengths of light. Ultraviolet and shaded light are also processed signals to the oscillator. Notably, the clock reciprocally generates rhythms of photoreceptor action leading to so-called gating of light responses. Intermediate proteins, such as Phytochrome interacting factors (PIFs), constitutive photomorphogenic 1 (COP1) and EARLY FLOWERING 3 (ELF3), have been established in signalling pathways downstream of photoreceptor activation. However, the precise details for these signalling mechanisms are not fully established. This review highlights both historical and recent efforts made to understand overall light input to the oscillator, first looking at how each wavelength of light is detected, this is then related to known input mechanisms and their interactions.</p>

For Review Only

1 Shining a light on the Arabidopsis circadian clock

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14 Abstract

15

16 The circadian clock provides essential timing information to ensure optimal growth to prevailing
17 external environmental conditions. A major time-setting mechanism (*zeitgeber*) in clock
18 synchronisation is light. Differing light wavelengths, intensities and photoperiodic duration are
19 processed for the clock-setting mechanism. Many studies on light-input pathways to the clock have
20 focused on *Arabidopsis thaliana*. Photoreceptors are specific chromic proteins that detect light
21 signals and transmit this information to the central circadian oscillator through a number of different
22 signalling mechanisms. The most well characterised clock-mediating photoreceptors are
23 cryptochromes and phytochromes, detecting blue, red and far-red wavelengths of light. Ultraviolet
24 and shaded light are also processed signals to the oscillator. Notably, the clock reciprocally
25 generates rhythms of photoreceptor action leading to so-called gating of light responses.
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27 photomorphogenic 1 (COP1) and EARLY FLOWERING 3 (ELF3), have been established in signalling
28 pathways downstream of photoreceptor activation. However, the precise details for these signalling
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31 detected, this is then related to known input mechanisms and their interactions.

32

Preprint
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33 The circadian clock

34 The circadian clock allows plants as sessile organisms to synchronise with diurnal changes in
35 the environment (Dodd *et al.*, 2005). Daily external environmental stimuli are required to initiate
36 circadian oscillations and to maintain synchronicity with the external environment. This process is
37 called entrainment. The environmental cues governing these processes are termed *zeitgebers* (from
38 German: "time givers"). The ability to synchronise with the external environment efficiently confers
39 enhanced fitness (Michael *et al.*, 2003).

40 Diurnal changes in cellular processes controlled by the clock allow plants to anticipate, and
41 therefore better survive, a range of stresses (Sanchez *et al.*, 2011). Diurnal changes have been
42 shown to occur in cold/freezing tolerance (Fornara *et al.*, 2015, Nakamichi *et al.*, 2009), drought
43 tolerance (Habte *et al.*, 2014), pathogen response (Shin *et al.*, 2012, Wang *et al.*, 2011) and
44 photosynthesis (Pyl *et al.*, 2012). This synchronisation is the product of a large number of
45 rhythmically regulated cellular processes (Bujdoso & Davis, 2013, Hanano *et al.*, 2008), many of
46 which are triggered by light perception (Wenden *et al.*, 2011). Perception of daily *zeitgebers*, such as
47 changes in light and temperature (Chow *et al.*, 2014, Harmer, 2009), enable plants to reset the clock
48 at dawn, and feed back to the central oscillator. For this light entrainment, photoreceptors play a
49 major role (Somers *et al.*, 1998a, Toth *et al.*, 2001). The circadian clock was derived from the
50 principle of inter-connected, positive and negative feedback loops (Shearman *et al.*, 2000). For the
51 purpose of this review, light input into the *Arabidopsis thaliana* (*Arabidopsis*) circadian clock will be
52 the focus of discussion, with a brief examination of clock components.

53 In *Arabidopsis*, morning expressed Myb-like transcription factors *CIRCADIAN CLOCK*
54 *ASSOCIATED 1 (CCA1)* (Wang & Tobin, 1998) and *LATE ELONGATED HYPOCOTYL (LHY)* (Schaffer *et al.*,
55 1998) antagonize expression of the evening expressed pseudo-response regulator (PRR) *TIMING OF*
56 *CAB EXPRESSION 1 (TOC1)* (Strayer *et al.*, 2000). These three genes form the core negative feedback
57 loop of the circadian oscillator (Alabadí *et al.*, 2001, Gendron *et al.*, 2012) (Figure 1). Several other
58 genes form additional loops within this core oscillator. In day time CCA1 and LHY repress expression
59 of the pseudo-response regulators *PRR5*, *PRR7* and *PRR9* (Adams *et al.*, 2015, Kamioka *et al.*, 2016),
60 as well as *TOC1*, *GI*, and the genes that generate the evening complex (Locke *et al.*, 2006, Nakamichi
61 *et al.*, 2009, Pokhilko *et al.*, 2010, Zeilinger *et al.*, 2006). *GIGANTEA (GI)* is evening expressed and is
62 proposed to form an additional negative feedback-loop with *TOC1* (Locke *et al.*, 2006). All of these
63 loops are connected through the action of the evening complex formed by *LUX ARRHYTHMO (LUX)*,
64 *EARLY FLOWERING 3 (ELF3)* and *EARLY FLOWERING 4 (ELF4)*, which directly inhibits the expression of
65 *PRR9* (Helfer *et al.*, 2011, Herrero *et al.*, 2012), *PRR7*, *GI* and *LUX* (Mizuno *et al.*, 2014). The absence
66 of even one component of the evening complex gives rise to plants that are photoperiod insensitive.
67 This results in early flowering, long hypocotyl growth and arrhythmicity of the free-running circadian
68 period (Hazen *et al.*, 2005, McWatters *et al.*, 2007, Onai & Ishiura, 2005, Thines & Harmon, 2010).
69 The importance of the three evening-complex components is thusly highlighted in maintaining a
70 functional circadian clock, and therefore the physiological processes controlled by the clock, such as
71 the input of diurnal photoperiod information, (Covington *et al.*, 2001, Más *et al.*, 2003, Mizoguchi *et*
72 *al.*, 2005, Park *et al.*, 1999).

73

74 Effects of light on the clock

75 Light changes throughout a day-night cycle are pronounced and thus robustly entrain the
76 clock. In the light phase of a daily cycle, the dark to light transition of dawn is used as a time setting
77 checkpoint (Millar *et al.*, 1995). Prolonged darkness causes many of the core genes in the
78 *Arabidopsis* central oscillator to rapidly become arrhythmic, due to the lack of essential light time
79 setting cues (Figure 2a) (Millar *et al.*, 1995). This dampening effect, leading to arrhythmicity is
80 particularly noticeable in the absence of media containing sucrose. In prolonged darkness, sucrose
81 can act as a substitute for light in maintaining rhythmicity for a number of days (Bläsing *et al.*, 2005).
82 Light has two main modes to set the clock. The first is parametric entrainment; gradual entrainment
83 of the clock, such as the acceleration of the clock induced by increased light perception, which

84 eventually leads to a phase shift of the clock back to a correct resonance. Parametric entrainment
85 follows Aschoff's rule, as light intensity increases, the speed of the clock increases. As intensity
86 decreases, the speed of the clock slows (Aschoff, 1979), (Figure 2B/C). Increases in light intensity,
87 lead to decreases in periodicity (Somers *et al.*, 1998a). The second light-induced time-setting
88 mechanism is non-parametric entrainment: rapid re-entrainment. This leads to a rapid time setting
89 of the clock at dawn (Millar & Kay, 1996). Non-parametric entrainment requires an extended light
90 exposure far beyond that which activates light-regulated gene expression (Millar & Kay, 1996).
91 Metabolic entrainment is also a mechanism for non-parametric entrainment (Haydon *et al.*, 2013,
92 Sanchez-Villarreal *et al.*, 2013; Haydon & Webb, 2016; Shin *et al.*, 2017). The different
93 photoreceptors and photochromic proteins involved in light entrainment are described in more
94 detail below.

95 96 How are different wavelengths of light input to the *Arabidopsis* clock?

97 Diurnal organisms, particularly plants, are subjected to Aschoff's rule: an increase in light
98 intensity accelerates the circadian-oscillator speed leading to shortening of periodicity (Aschoff,
99 1979). Light input to the circadian clock is presumed to occur through the action of different types of
100 photoreceptors (Somers *et al.*, 1998a). There are more than ten known circadian-associated
101 photoreceptors (Edwards *et al.*, 2015). These can be split into four classes: phytochromes,
102 cryptochromes, ZTL/FKF1/LKP2 family, and UVR8. Each receptor contributes in the dose-dependent
103 perception of far-red, red, blue, and ultra-violet light (Cashmore *et al.*, 1999, Mas *et al.*, 2000, Rizzini
104 *et al.*, 2011, Song *et al.*, 2012). It is presumed that the input of this information is co-ordinately
105 relayed to the central oscillator.

106 Both phytochromes and cryptochromes play key roles in light responsive time setting
107 mechanisms, in a manner that follows Aschoff's rule (Devlin & Kay, 2000a, Somers *et al.*, 1998a). This
108 is due to the ability of both phytochromes and cryptochromes to form photoreceptor complexes
109 (Más *et al.*, 2003) that are genetically interactive in clock function (Devlin & Kay, 2000a). Excitation
110 of these photoreceptors cause the central oscillator to accelerate, changing the overall speed of the
111 clock (Devlin & Kay, 2000b, Herrero *et al.*, 2012, Kolmos *et al.*, 2011, Somers *et al.*, 1998a, Somers
112 *et al.*, 1998b). There are a number of different known mechanisms through which light absorption by
113 photoreceptors input environmental information to the oscillator, however, these mechanistic
114 details are not complete. Regulation of transcription by circadian gating restricts changes in RNA
115 levels to specific times of day. Therefore preventing transcription of some light-regulated clock
116 genes in response to unexpected external stimuli, for example light pulses during the night (Millar &
117 Kay, 1996). Light regulation of myb transcription factors, such as *CCA1* and *LHY* effect the
118 transcription and stability of other clock components, such as *PRR9/7* (Carre & Kay, 1995).
119 Messengers such as Ca^{2+} and calmodulin signalling may also affect circadian regulation in response to
120 light (Johnson *et al.*, 1995, Millar & Kay, 1996). Light also directly controls the degradation of *PRR5*,
121 *PRR7*, *PRR9*, *TOC1* and *GI* proteins (Farré and Kay, 2007, Ito *et al.*, 2007, Kiba *et al.*, 2007, Más *et al.*,
122 2003, Matsushika *et al.*, 2000). These degradation events then act on outputs within a diurnal
123 context, which change in duration throughout the season (Davis, 2002, Guerriero *et al.*, 2012,
124 Salazar *et al.*, 2009, Song *et al.*, 2012, Troein *et al.*, 2009). Light thus has multiple mechanistic inputs
125 to clock processes, all of which control entrainment. How each individual wavelength of light is input
126 to the clock will be discussed below.

127 128 Red light

129 Phytochromes are predominantly red-light photoreceptors, absorbing maximally at
130 wavelengths between 600 and 700nm (Somers *et al.*, 1998a). *Arabidopsis* has five phytochromes
131 (Sharrock & Quail, 1989), phyA-phyE (Mathews & Sharrock, 1997). Each phytochrome acts as a light
132 input sensor to form regulatory feedback loops within the circadian clock. Phytochromes are in turn
133 reported to be negatively regulated by the clock through cryptochrome (CRY) signals (Devlin & Kay,
134 2000a, Mas *et al.*, 2000). Phytochromes exist in two interconvertible forms; the inactive Pr form is

135 converted by red light to the active Pfr form which can be converted back to the inactive Pr state by
136 far-red light (Rudiger *et al.*, 1983). These conversion events between active and inactive forms of
137 phytochrome are essential to light input to the clock, as discussed below (see far red, PIFs, ELF3).
138 Each of the five phytochromes play distinct roles in light sensing.

139 phyA mediates entrainment responses to low intensity red light and pulses of light (Quail *et al.*
140 *et al.*, 1995, Somers *et al.*, 1998a). A *PHYA* deficiency mutation, results in an altered period length in
141 dim red light (Somers *et al.*, 1998a). It is not known how phyA signals to the clock as it has not been
142 reported to directly bind to a clock-associated factor, in contrast to the other four phytochromes
143 (Huang *et al.*, 2016).

144 phyB is the main detector for high intensity red light (Somers *et al.*, 1998a). Both phyB and
145 phyD are able to detect red and far-red wavelengths of light (Aukerman *et al.*, 1997, Devlin *et al.*,
146 1999). phyB physically interacts with ELF3 in the central oscillator to provide a direct light input to
147 the clock (Kolmos *et al.*, 2011, Liu *et al.*, 2001). *phyb* mutants show an altered response to shade
148 avoidance (Smith, 1995), which is also a phenotype of the *elf3* mutant (Huang *et al.*, 2016). phyC to
149 phyE also interact with ELF3 protein (Huang *et al.*, 2016), but this has not yet been connected to the
150 clock (Liu *et al.*, 2001). Under high fluence red light, *phyb* mutants and the phyB overexpressor have
151 a period defects and altered phase (Anderson *et al.*, 1997, Kolmos *et al.*, 2011, Salomé *et al.*, 2002,
152 Somers *et al.*, 1998a). Also altered cryptochrome signalling (see blue light below), phyB and CRY2
153 physically interact by translocating to the nucleus in red light (Mas *et al.*, 2000), where phyB is then
154 suppressed by CRY2 (Mas *et al.*, 2000). This alters clock performance under white light conditions (red
155 and blue light together) (Devlin & Kay, 2000a).

156 In non-peer-reviewed work, phyC was found to play a role in white-light input and red-light
157 detection. Mutations in *PHYC* result in a long-period phenotype, which was shown to be
158 temperature dependant, suggesting that phyC inputs not only light information to the clock, but also
159 temperature (Edwards *et al.*, 2015, Franklin *et al.*, 2003, Qin *et al.*, 1997). phyE along with phyD plays
160 a role in controlling the period length of *CAB* gene expression, however, many of the clock effects of
161 phyE and phyD are masked by phyB (Franklin & Quail, 2010). phyE works with phyB and phyD in the
162 regulation of shade avoidance (Devlin *et al.*, 1998). Interestingly, the promoters of *PHYA* and *PHYB*
163 are down-regulated by light, whereas the *PHYC* promoter is upregulated (Tóth *et al.*, 2001), *PHYD*
164 and *PHYE* do not show changes in expression in response to light changes. *PHYB,D,E* mediate high
165 fluence red light input to the clock with *PHYA,B,D,E* acting additively to input red-light information to
166 the clock, as a result the clock runs faster as the detected intensity of red light increases (Devlin &
167 Kay, 2000a). The absence of all five phytochromes results in severally attenuated rhythms, but not a
168 total loss of clock function (Hu *et al.*, 2013). Together, all five phytochromes play differing roles in
169 mediating light-dependant changes in periodicity.

170

171 Blue light

172 Cryptochromes are blue light (492 to 455nm) and UVA photoreceptors present in both
173 plants and animals (Cashmore *et al.*, 1999). The *HY4* locus was found to encode cryptochrome 1
174 (CRY1). It was identified due to *cry1* (*hy4*) mutants growing with a long-hypocotyl phenotype and
175 being unable to respond to blue light (Ahmad & Cashmore, 1993, Koornneef *et al.*, 1980), *cry1/hy4*
176 plants are also late flowering (Goto *et al.*, 1991, Millar *et al.*, 1995). *cry1* mutants have a long period
177 under blue light (Somers *et al.*, 1998a), suggesting CRY1 acts as a photoreceptor for blue-light
178 entrainment of the clock (Devlin & Kay, 2000a). Overexpression of *CRY1* caused increased sensitivity
179 to blue light and period shortening (Lin *et al.*, 1996, Somers *et al.*, 1998a). CRY1 is a soluble protein
180 when grown in both light and dark conditions in *Arabidopsis* (Lin *et al.*, 1996), CRY1 is more stable
181 than CRY2 and works at higher light intensities (Lin *et al.*, 1998). Cryptochrome 2 (CRY2) can detect
182 low intensity light and is rapidly degraded under blue light (Lin *et al.*, 1998). In light, *CRY2* promoter
183 activity is down-regulated whereas, *CRY1* is upregulated (Tóth *et al.*, 2001). The *cry2* mutation alters
184 sensitivity to photoperiod and flowering in *Arabidopsis*, but does not have a detectable individual
185 effect on circadian rhythm (Devlin & Kay, 2000a, Guo *et al.*, 1998). Overexpression of either *CRY1* or

186 *CRY2* gives rise to a higher blue-light sensitivity under low light conditions than in the individual
187 overexpression lines (Ahmad *et al.*, 1998a). Double mutant *cry1, cry2* plants are rhythmic, suggesting
188 that although *CRY1* inputs blue light into the clock *CRY1* and 2 are not part of the central oscillator
189 (Devlin & Kay, 2000a). However, *CRY1* and *CRY2* gene expression oscillates with a circadian rhythm
190 under constant light (Harmer *et al.*, 2000). *CRY1* and 2 work together to input information to the
191 clock in a similar way to *phyA* and *B*, but at differing light intensities.

192 Phytochromes are able to absorb low fluence blue light alongside *CRY1* for period length
193 control. *phyA* mutants show a period lengthening effect when free run under blue light (Somers *et al.*,
194 1998a). Without *phyA* detection of blue light, the input relies on *CRY1* alone causing the period
195 to lengthen as the plant detects less light than the actual ambient intensity of irradiation.
196 Conversely, *PHYA* overexpression has been proposed to cause period shortening under blue light, as
197 more blue light is processed as an input than the actual ambient light intensity. Phytochromes thus
198 also work in blue-light signalling to the clock.

199

200 High light synergism - (White light)

201 White light comprises of multiple light wavelengths. As such, interactions between
202 phytochromes and cryptochromes are needed to input this information into the circadian clock.
203 These interactions were found with loss of function mutants for both phytochromes and
204 cryptochromes. In wild-type plants *CAB2* period decreases as light intensity increases, *cry2* mutants
205 were found to be deficient in a white light response as they have a *CAB2* period increase in response
206 to high light (Mas *et al.*, 2000). This period increase was not detected in either red or blue light
207 alone, suggesting that to be active *CRY2* needs multiple wavelengths of light simultaneously and
208 *phyB* (Mas *et al.*, 2000). *CRY1* was also found to be required for *phyA* signalling as *cry1* and *cry2*
209 mutants are unable to detect red light above the fluence range of both *phyA* and *phyB* (Devlin & Kay,
210 2000a). Light induces nuclear compartmentalisation of phytochromes where *phyA* and *phyB* directly
211 interact with *CRY1* and *CRY2* (Mas *et al.*, 2000), the kinase activity of *phyA* phosphorylates *CRY1* and
212 *CRY2* (Ahmad *et al.*, 1998b).

213 Phytochromes and cryptochromes facilitate signal integration of multiple light cues. *CRY2* is
214 activated when illuminated by multiple wavelengths of light suggesting it is needed for phytochrome
215 activation (Mas *et al.*, 2000). This is also highlighted as both cryptochromes reach peak RNA
216 expression with a similar expression pattern to the corresponding phytochromes (Toth *et al.*, 2001).
217 It was found that the active Pfr form of phytochrome is needed for *CRY2* expression, *CRY2* then
218 suppresses *PHYB* expression. However, PfrB is able to override *CRY2* signalling to flowering time
219 control via pathways, such as *COP1* (see below). PfrB binding to the intermediate *SPA1* allows
220 degradation of the *COP1-SPA1* complex, which is needed as an intermediate of *CRY1/2* induced
221 inhibition of photomorphogenic factors such as *HFR* and *CO* (Mas *et al.*, 2000, Sheerin *et al.*, 2015).
222 Additionally, both *CRY1* and *CRY2* were found to be phosphorylated by the kinase activity of *phyA*
223 (Ahmad *et al.*, 1998b). It could be considered that phytochromes and cryptochromes work together
224 in the "white light" response, which is a more than the additive effect of plants grown under blue
225 and red light. However, quadruple mutants for *phyA, phyb, cry1* and *cry2* still showed rhythmic leaf
226 movement in response to light-dark cycles suggesting that other photoreceptors must play a role in
227 overall light input to the circadian clock (Yanovsky *et al.*, 2000). However, the exact relationship
228 between phytochromes and cryptochromes is yet to be resolved.

229

230 ZTL family; blue-light absorbing with action under red-light and darkness

231 *Zeitlupe* (*ZTL*), also reported as *ADAGIO1* (*ADO1*), links light input by both cryptochromes
232 and phytochromes to the clock (Jarillo *et al.*, 2001, Kim *et al.*, 2007). *ZTL* mutant lines showed
233 altered cotyledon movement and gene expression under different light conditions (Jarillo *et al.*,
234 2001). Under blue and white light, *ztl* plants have a long period whereas under red light the *ztl* lines
235 were reported to be arrhythmic for *CCR2* expression, cotyledon movement and stem elongation
236 (Jarillo *et al.*, 2001). *ZTL* mutants were found to have a long-period phenotype for *CAB/TOC1* under

237 red light (Kevei *et al.*, 2006, Kim *et al.*, 2005). ZTL thus is required for the perception of multiple
238 wavelengths of light into the oscillator.

239 ZTL encodes a protein reported to be a blue-light photoreceptor, as it contains a PAS
240 domain, F box domain linking proteins to a SCF ubiquitination complex, kelch repeats and a light,
241 oxygen or voltage (LOV) domain allowing protein-protein interactions (Mas *et al.*, 2003). Interactions
242 between TOC1 and ZTL were found to occur through these kelch-repeat zones (Kevei *et al.*, 2006).
243 The PAS/ LOV domain were identified as essential for coupling ZTL to red light (Kevei *et al.*, 2006),
244 which was then found to occur through ZTL binding to the C-terminus of PhyB and CRY1 (Kim *et al.*,
245 2007).

246 ZTL is constitutively expressed at the RNA level, however, oscillations in ZTL protein levels
247 are seen (Kim *et al.*, 2007). These are proposed to result from the binding of Gigantea (GI) to
248 maintain the stability of ZTL. ZTL protein folding is chaperoned by HSP90 (Kim *et al.*, 2011), GI binds
249 to the ZTL-HSP90 complex to ensure specificity of protein folding (Cha *et al.*, 2017, Kim *et al.*, 2011).
250 interactions between ZTL and GI are enhanced by blue light through the LOV domain in ZTL (Kim *et al.*
251 *et al.*, 2007). ZTL controls proteasomal degradation of TOC1 (Más *et al.*, 2003). This ZTL-GI interaction
252 is believed to control a central part of the circadian oscillator. ZTL and ELF3 were reported to have
253 opposite effects on clock function. *ztl* mutants and *ELF3* overexpression lines show a lengthened
254 circadian period in light. Conversely *elf3* mutants and ZTL overexpression lines are reported as
255 arrhythmic under constant light (LL) (Kim *et al.*, 2005). However, the *elf3-ztl* double mutant showed
256 that ELF3 and ZTL have additive effects on the clock (Kim *et al.*, 2005). As GI controls the HSP90
257 mediated stabilisation of ZTL protein (Cha *et al.*, 2017, Kim *et al.*, 2011), ZTL protein then causes
258 protein depletion of TOC1 via ubiquitination (Kim *et al.*, 2011). ELF3 interacts as a substrate adaptor
259 for COP1 (an E3 ubiquitin ligase) to bind to and degrade GI protein, as a light input signal and
260 indicator of day length in response to CRY2 (Yu *et al.*, 2008). The reduction of GI then prevents the
261 formation of stable ZTL protein. Consequently this prevents ZTL-mediated inhibition of TOC1 in the
262 central oscillator, and facilitates TOC1 action. ZTL also negatively regulates PRR5 by targeting PRR5
263 protein for degradation via the 26S proteasome (Fujiwara *et al.*, 2008, Kiba *et al.*, 2007). As PRR5
264 forms a negative regulatory feedback loop with LHY/ CCA1, ZTL therefore indirectly plays a role in
265 the regulation of LHY/CCA1 within the central oscillator (Baudry *et al.*, 2010).

266

267 Far-red light

268 *phyA* is the presumed photoreceptor for detecting monochromatic far-red light. Mutations
269 in *PHYA* resulted in loss of capacity for clock function (Wenden *et al.*, 2011). ELF4 was proposed to
270 restrict far-red perception in those studies. Interestingly, the active form of *phyA* (*phyA-Pfr*) is
271 formed under far-red light (Clough & Vierstra, 1997), given that far red converts the Pfr form of
272 phytochrome back to the inactive Pr form. In part perhaps *phyA* evolved the ability to form Pfr under
273 far red as a response to the change in light quality at the end of the day, which signals the transition
274 from day to night and therefore the associated changes in environment. However, far red can also
275 be a signal of shade due to far red being one of the only wavelengths of light able to pass through
276 leaves (Federer & Tanner, 1966), suggesting that there may be different mechanisms to entrain the
277 clock in these two different circumstances, as described in the next section. Plants in constant far-
278 red light have a faster clock and show high expression of evening genes, such as *PRR1/TOC1*, and low
279 expression of the morning genes *CCA1* and *LHY* (Wenden *et al.*, 2011). The exact mechanism of far-
280 red input to the clock is not fully characterised. However, far red has been shown to be involved in
281 the prevention of the interaction between Pfr and PIF3 (Martínez-García *et al.*, 2000). ELF4 was
282 identified as playing a role in mediating far-red light input to the clock (Wenden *et al.*, 2011), Far-red
283 light was used to aid recovery of rhythmicity in the otherwise arrhythmic *elf3* and *elf4* mutants
284 (Kolmos *et al.*, 2011, Wenden *et al.*, 2011).

285

286 Shaded light

287 White light with supplementary far-red light causes the clock to slow down (Jiménez-Gómez
288 *et al.*, 2010). Under shade, far red and potentially green light are present; there is a large overlap
289 between far-red signalling and shade. Shade however, is a useful environmental indicator to plants
290 for neighbour detection. *phyA* is thought to have the most involvement in mediating far-red
291 signalling, but *phyB* also plays a key role (Kolmos *et al.*, 2011, Wenden *et al.*, 2011). Shading plants
292 during the afternoon was found to have the greatest effect (Sellaro *et al.*, 2012). Responses to shade
293 involve the degradation of phytochrome interacting factors, namely PIF4 and 5 (Lorrain *et al.*, 2008).
294 PRR5 was found to regulate the shade-avoidance response by controlling PIF4 and PIF5, as well as
295 downstream components of the phytochrome-mediated signalling pathway. Furthermore ZTL
296 induces degradation of PRR5. However, this degradation was found to be repressed under blue light.
297 It was suggested that PRR5 gates phytochrome mediated shade responses (Takase *et al.*, 2013). *ELF3*
298 and *LUX* mutants (both components of the evening complex) show a reduced response to all
299 wavelengths of light therefore growing with elongated hypocotyls as though under shade (Jiménez-
300 Gómez *et al.*, 2010, Sellaro *et al.*, 2012, Zagotta *et al.*, 1996). This implies that *ELF3* and the evening-
301 complex also play a role in the shade response to the clock (Kolmos *et al.*, 2011).

302

303 UV-B light

304 Ultraviolet B light (UVB) can be one of the more damaging wavelengths present in sunlight.
305 UVB is a wavelength that is easily absorbed and damages both DNA and proteins (Jansen *et al.*,
306 1998), thus making UVB a useful light signal, but at the cost of inducing a stress response. UVB is an
307 "anti-shade" signal informing a plant it is under direct sunlight. At lower-fluence rates, UV-B light is
308 able to control development, promote photomorphogenesis, and drive gene expression (Heijde &
309 Ulm, 2012). *Ultraviolet resistance locus 8 (UVR8)* drives signalling for the majority of UVB responses
310 (Favory *et al.*, 2009, Rizzini *et al.*, 2011). Under UVB light, COP1 promotes the induction of elongated
311 hypocotyl 5 (HY5) and HY5 homologue (HYH) which induce stress responses such as flavonoid
312 biosynthesis to reduce UVB induced damage (Stracke *et al.*, 2010). UVR8 and COP1 are also crucial
313 for UVB light entrainment of the clock (Fehér *et al.*, 2011). Under white light supplemented with UV-
314 B light, COP1 induces HY5 and HYH, HY5 and HYH have not yet been implicated for clock
315 entrainment by UVB (Fehér *et al.*, 2011). UVR8 is able to mediate both parametric and non-
316 parametric entrainment, by inducing *PRR9* and *GI* under continuous light, alongside an increase in
317 *CCA1* and *ELF3* response to UVB light pulses. UVR8 was identified as the UVB receptor that can
318 mediate signal input to the oscillator, due to the fact that *uvr8* plants cannot input UVB light into the
319 oscillator, (Fehér *et al.*, 2011, Heijde & Ulm, 2012). It has been proposed that UVR8 mediates UVB
320 light input into the central oscillator by inhibiting PIF4 in the presence of UVB light. This requires
321 COP1-mediated repression of *PIF4* transcript, and also through the stabilisation of HFR, which
322 inhibits PIF4 (Hayes *et al.*, 2017). Canonical pathways used in UVB signalling mediate entrainment in
323 the clock, but the critical nodes in entrainment are not fully resolved (Hayes *et al.*, 2017).

324

325 Green light

326 Many studies have been carried out to test the physiological effects that occur as a
327 consequence of increased or absent green-light wavelengths. The mechanisms of sensing and input
328 to the circadian clock are yet to be understood. It is thought that green wavelengths can operate via
329 both a cryptochrome dependant and independent pathway (Folta & Maruhnich, 2007). Green light
330 can reverse the effect of blue light on hypocotyl elongation (Bouly *et al.*, 2007, Folta, 2004),
331 potentially due to the reversal of the blue light degradation of CRY1 (Bouly *et al.*, 2007). This could
332 then have an effect on photoperiod and subsequently flowering time (Banerjee *et al.*, 2007, Folta &
333 Maruhnich, 2007). The association of green light to cryptochromes was also shown by (Lin *et al.*,
334 1996) as overexpression of CRY1 causes increased sensitivity to green light. A reversible interaction
335 between CRY and green light similar to that found for phytochrome in red and far red light suggests

336 that there are intermediate signalling factors similar to PIFs that are yet to be identified. It is thus
337 plausible that green light could entrain the clock, but no definitive experiments have tested this.

338

339 Transcriptional regulation of photoreceptors by the clock.

340 The circadian clock generates rhythms of RNA and/or accumulation for all photoreceptor
341 classes. Starting with the discovery that *phyB* mRNA is rhythmic (Bognár *et al.*, 1999, Toth *et al.*,
342 2001, Tóth *et al.*, 2001), subsequent findings revealed that all five phytochromes in Arabidopsis
343 cycle. Interestingly, sub-nuclear accumulation of phytochrome holoprotein also appears to be under
344 clock control. However, the implications of this are currently unclear. Similarly, *CRY* genes are
345 rhythmic (Toth *et al.*, 2001). For *UVR8*, as UV light induces dimer disassembly to a monomer state, a
346 diel cycle of dimers at night and monomers during the day occur (Findlay & Jenkins, 2016). *UVR8*
347 mRNA displays robust circadian rhythms with a peak around subjective dusk (Mockler *et al.*, 2007).
348 For *ZTL*, the mRNA generated does not cycle, but robust protein cycling is readily detectable.
349 Together it is clear light receptors that act as input components to the clock, are themselves
350 circadian-output regulated.

351

352 Phytochrome input to the central oscillator

353 Light input to the central oscillator is a daily *zeitgeber*, but the central oscillator also acts as a
354 feedback mechanism to phytochromes over the day. The oscillator receives a number of light queues
355 during the light phase of each day from photoreceptors detecting the different ratio of light
356 wavelengths across the day. In turn, the oscillator inhibits expression of phytochrome proteins at
357 points hypothesised in Figure 3.

358 At dawn (ZT0), *PHYC* peaks with the return of light and changing temperature (Toth *et al.*,
359 2001). HFR increases due to increased stability (Yang *et al.*, 2005). PIF4/5 expression peaks at dawn
360 (Nomoto *et al.*, 2012), due to the lack of phytochromes, thus preventing phytochrome-induced
361 degradation at dawn (Shin *et al.*, 2013). PIF4/5 continue to be present throughout the light phase,
362 but are slowly degraded by interactions with the Pr form of phytochrome, PIFs can also interact with
363 LHY, CCA1. PfrB interacts with PIF3, where PIF3 then binds to the G-box domain of *CCA1/LHY*
364 promoters. CCA1 and LHY, as MYB transcription factors, then control other genes within the central
365 oscillator, such as *PRR5*, 7 and 9, as well as non-circadian genes (Martínez-García *et al.*, 2000, Wang
366 & Tobin, 1998).

367 *PHYD* and *E* are expressed two hours after dawn (Toth *et al.*, 2001). During the first half of
368 the light phase (ZT0-6) there is an increase in light intensity up to ZT6, and alongside this, an
369 increasing expression of phytochromes. *PHYB* and *CRY1* reach peaks in expression around mid-day
370 (ZT6) as both *phyB* and *CRY1* work at high-light intensities (Lin *et al.*, 1996, Lin *et al.*, 1998, Toth *et al.*,
371 2001). *CAB1* expression peaks around mid-day as does the expression of HFR (Yang *et al.*, 2005).
372 HFR is thought to interact with PIF3 (Fairchild *et al.*, 2000), but the mechanism through which this
373 happens is not fully understood.

374 Both *PHYA* and *CRY2* peak towards the latter half of the light phase (ZT6-12) with the
375 decreasing light and increasing far red intensity (Toth *et al.*, 2001). *CRY2* detects lower intensity light
376 (Lin *et al.*, 1998), and the Pfr form of phytochrome is needed for *CRY2* activation (Mas *et al.*, 2000).
377 *CRY2* then suppresses *PHYB* expression (Mas *et al.*, 2000). *phyA* is essential in controlling the clock in
378 low light (Quail *et al.*, 1995, Somers *et al.*, 1998a) and far red conditions (Wenden *et al.*, 2011),
379 potentially through the Pfr form of phytochrome being unable to interact with PIF3 (Martínez-García
380 *et al.*, 2000).

381 At dusk, *CAB2* expression decreases, and *COP1* expression increases (Yang *et al.*, 2005),
382 allowing *COP1* suppression of HFR throughout the dark phase of the day. *COP1* accumulation along
383 with *ELF3* inhibits *GI* late in the afternoon (Yu *et al.*, 2008). *PILs* are rapidly produced during the first
384 hour of shade, early into the dark phase and work with *TOC1* to restrict growth (Salter *et al.*, 2003).
385 *PIF3* is at its highest level at dusk due to its interactions with the Pfr form of phytochrome and the
386 highest level of Pfr being present just before dusk. Allowing information on high levels of far red light

387 to be input to the central oscillator (Martínez-García *et al.*, 2000). The evening complex (ELF3, ELF4,
388 LUX) inhibits the transcription of *PIF4/5* at dusk (Herrero *et al.*, 2012, Nusinow *et al.*, 2011; Raschke
389 *et al.* 2015). This allows PIF protein to accumulate stably due to the lack of phytochrome inhibition
390 overnight, which thus promotes growth, reaching a maximal level at dawn (Shin *et al.*, 2013, Delker
391 *et al.* 2014; Raschke *et al.* 2015).

392

393 COP1

394 Constitutive photomorphogenic 1 (COP1) is an E3 ubiquitin ligase, mediating day length
395 input to the clock and flowering time. COP1 is negatively regulated by a direct protein-protein
396 interaction with CRYs (Jang *et al.*, 2008, Wang *et al.*, 2001, Yang *et al.*, 2000). *phyA* and *B* affect the
397 nuclear abundance of COP1 (Osterlund *et al.*, 1999), as the C-terminal domain of *phyB* directly
398 interacts with COP1 (Millar *et al.*, 1994). COP1 acts as an intermediate, inputting photoperiodic
399 information from PHY and CRY into the oscillator. COP1 in turn plays a negative regulatory role
400 targeting *phyA*, *phyB* and HFR1 for ubiquitination (Osterlund *et al.*, 2000, Seo *et al.*, 2003, Yang *et al.*,
401 2005).

402 CRY1, CRY2, *phyA* and *phyB* all interact with COP1 via Suppressor of Phytochrome A (SPA).
403 SPA1 is a nuclear localised repressor of phytochrome signalling (Hoecker *et al.*, 1999), which
404 interacts with COP1 (Hoecker & Quail, 2001). SPA1 contains a coiled-coil domain that enhances the
405 E3 ligase activity of COP1 on its targets (Seo *et al.*, 2003). The interactions between the 4 known SPA
406 proteins and COP1, negatively regulate light signalling in response to certain wavelengths of light
407 (Laubinger *et al.*, 2004, Zhu *et al.*, 2008). COP1-SPA1 interaction is repressed by activated CRY1 in
408 blue light (Lian *et al.*, 2011), CRY2 interacts with COP1 via SPA1 to allow COP1 proteolysis of CO to
409 control flowering time under blue light (Zuo *et al.*, 2011). The CRY1-SPA1 interaction enhances CRY2-
410 SPA1 activity in response to blue light to suppress COP1 activity resulting in a suppression of CO
411 degradation (Ordoñez-Herrera *et al.*, 2015, Zuo *et al.*, 2011).

412 In seedlings, *phyA* binds to SPA1 and 2 whereas, in adult plants *phyA* binds to SPA3 and 4
413 (Laubinger *et al.*, 2004). Binding of *phyB* to SPA1 is Pfr dependant allowing degradation of
414 COP1/SPA1 in light conditions that promote nuclear accumulation of *phyA* and *B*, this enhances light
415 responses, as the disruption of COP1/SPA1 interaction prevents degradation of photomorphogenic
416 factors such as HFR, and HY5 (Sheerin *et al.*, 2015). The COP1/SPA complex is an important factor in
417 repression of light responses in darkness, as the COP1/SPA complex interacts directly with
418 photoreceptors leading to its inactivation (Huang *et al.*, 2014).

419 Within the central oscillator, COP1 interacts with ELF3 to mediate COP1 degradation of GI
420 late in the afternoon (Yu *et al.*, 2008), potentially using ELF3 as an adaptor for COP1 binding to GI
421 (Liu *et al.*, 2008). It is also possible that COP1 regulates the level of ELF3 present, in *cop1* mutants
422 ELF3 protein accumulates to higher levels than in the wild type, but the mRNA levels remain
423 unchanged (Liu *et al.*, 2001).

424 COP1 is also involved in UVB signalling as *cop1* mutants are deficient in a UVB response
425 (Oravec *et al.*, 2006). In the early stage of UVB signalling, UVR8 and COP1 directly interact in the
426 nucleus (Favory *et al.*, 2009), UVR8 and COP1 were found to be essential for UVB entrainment (Fehér
427 *et al.*, 2011). HY5 and HYH which are also important components of UVB signalling are regulated by
428 COP1 (Brown & Jenkins, 2008). In the light COP1 detaches from HY5 allowing stabilisation and the
429 light responsive target genes of HY5 to be activated (Yi & Deng, 2005). COP1 plays an important
430 mediator role in the input of light from photoreceptors to the oscillator. In turn its regulation is
431 dependent on photoreceptors, the short-period phenotype in mutant lines shows that COP1 plays a
432 negative regulatory role on the clock.

433

434 PIFs and PILs

435 Phytochrome interacting factors (PIF) are a family of basic helix loop helix transcription
436 factors. There are 4 well characterised PIFs, PIF1,3,4,5 (Leivar *et al.*, 2012). (Pfeiffer *et al.*, 2012) PIFs
437 are unstable in the light due to their interaction with active phytochrome causing phosphorylation

438 and subsequent degradation (Leivar *et al.*, 2012, Soy *et al.*, 2012). The most well characterised PIF is
439 PIF3, which was found to interact with the Pfr form of phytochrome B (PfrB) acting as a bridge
440 between PfrB and its target gene by translocating PfrB to the nucleus. Thus allowing light induced
441 control of gene expression, as PIF3 does not interact with the Pr form of phytochrome (Martínez-
442 García *et al.*, 2000, Pfeiffer *et al.*, 2012). PIFs are also able to input information to the clock via direct
443 interaction with clock genes that contain a G-box motif in their promoter, PIFs can interact directly
444 with *LHY*, *CCA1*, *PRR5*, *PRR7*, *PRR9* and *LUX* (Martínez-García *et al.*, 2000). This is potentially one of
445 the main mechanisms through which light/ day length information is used to control or alter the
446 clock. The central oscillator in turn regulates PIF expression. Postdusk, *TOC1* peaks in expression,
447 allowing direct interactions between *TOC1* and PIF3, which results in the *TOC1* gating of PIF induced
448 growth, until *TOC1* levels decrease predawn (Soy *et al.*, 2016).

449 *PIF4* and *5* show rhythmic expression with a diurnal peak at dawn (Nomoto *et al.*, 2012).
450 Expression of *PIF4* and *5* is controlled by the evening complex, comprising of *ELF3*, *ELF4* and *LUX*
451 (Herrero *et al.*, 2012), which binds to the promoter region of *PIF4* and *5* to inhibit transcription at
452 dusk (Nusinow *et al.*, 2011). PIF protein stably accumulates overnight due to the lack of
453 phytochrome induced degradation to reach their maximum level at dawn (Shin *et al.*, 2013). As PIFs
454 are growth-promoting factors (Shin *et al.*, 2013), this leads to the highest growth rate occurring at
455 the end of the night phase.

456 PIFs may also input information from other environmental cues to the clock such as
457 temperature (McClung & Davis, 2010; Raschke *et al.* 2015). It was shown that *PIF4* expression also
458 increases in response to temperature increases (Shin *et al.*, 2013). As dawn induces a temperature
459 increase, alongside the return of daylight it would perhaps be advantageous to a plant to be able to
460 input both of these environmental cues into the clock at the same time.

461 PIF3 like (PILs) are also basic helix loop helix transcription factors with large overlaps in
462 function to PIFs, but have been associated with shade avoidance (Li *et al.*, 2014). This overlap in
463 function has led to some ambiguous nomenclature as *PIL5* is also referred to as *PIF1* and likewise
464 *PIL6* as *PIF5* (Li *et al.*, 2014). *PIL1* has a distinct function and was shown to work with *TOC1* to restrict
465 growth at specific times of day (Salter *et al.*, 2003). *PIL1* accumulates rapidly within the first hour of
466 shade cover acting as part of a rapid signalling pathway to stop growth (Li *et al.*, 2014), a secondary
467 longer lasting shade response is then mediated by *HFR* and phytochrome rapidly regulated (*PAR1/2*)
468 (Galstyan *et al.*, 2011). The exact mechanism through which *PIL1* halts growth in shade is not known
469 but a number of hypothesis were presented in (Li *et al.*, 2014). It was suggested that as *PIF1* has a
470 binding site for phyB it is possible that in shade *PIL1* may outcompete PIF for DNA binding sites on
471 the Pfr form of phyB, therefore reducing the growth promoting function of *PIF5* (Li *et al.*, 2014).
472 Alternatively, *PIL1* may work via a PIF independent mechanism on components of downstream
473 pathways; however this is yet to be tested.

474

475 HFR

476 Long hypocotyl in far red 1 (*HFR1*) is a basic helix loop helix transcription factor involved in
477 phytochrome-mediated signalling (Fairchild *et al.*, 2000), and photomorphogenesis (Yang *et al.*,
478 2005). *HFR* is unstable in darkness and accumulates in the light, this accumulation is due to light
479 preventing *COP1* mediated degradation of *HFR* (Yang *et al.*, 2005). *HFR* is not able to bind phyA or B
480 directly, instead *HFR* binds *PIF3* forming potentially a heterodimer of *PIF3/HFR* which can then bind
481 to the Pfr form of phyA/B. This is also highlighted by the fact that *HFR* is more abundantly found in
482 far red light (Fairchild *et al.*, 2000). Mutants deficient in *HFR* had defective phyA responses, such as
483 hypocotyl elongation, and induction of chlorophyll A binding protein (*CAB*) (Fankhauser & Chory,
484 2000). *HFR* is also thought to have a blue-light response (Duek & Fankhauser, 2003) through *CRY1*
485 (Yang *et al.*, 2005), but the exact mechanism through which this occurs is not known.

486

487 Intersection of the clock components ELF3- and ELF4 to light and clock signalling: major integrators
488 of light to the clock

489 *EARLY FLOWERING 3 (ELF3)* was first identified as a negative regulator of flowering time. In
490 addition to the observation that *elf3* mutant was shown to be early flowering, large circadian defects
491 were identified (Hicks *et al.*, 1996, Roden *et al.*, 2002; Undurraga *et al.*, 2012). *elf3* mutants are
492 defective in gating of red-light perception to the clock. Cloning of ELF3 allowed for interactors to be
493 detected, phyB was revealed to be a factor that associated to the N-terminus of ELF3 (Liu *et al.*,
494 2001). ELF3 was identified as playing a role in light signalling, in 12hours light 12 hours dark
495 entrainment, ELF3 accumulates in the nucleus just before darkness (ZT12) (Liu *et al.*, 2001).
496 Increasing day length, increases the nuclear accumulation of ELF3, increased darkness causes
497 accumulation of ELF3 to decrease to an undetectable level (Liu *et al.*, 2001) showing a direct
498 relationship between light and ELF3.

499 Phase response curves are made by measuring circadian period and phase during light
500 pulses, at times across subjective day and night. Phase response curves for wild-type Arabidopsis in
501 both red and blue light show the greatest effect and subsequent clock resetting to be caused by a
502 light pulse during the subjective night. *ELF3* overexpression lines showed a much more gradual
503 change in phase response with the same light pulses (Covington *et al.*, 2001). In white light, *ELF3*
504 overexpression causes a period lengthening effect in a light-dependent manner. In darkness, the
505 oscillator pace is not altered (Covington *et al.*, 2001). In *elf3* mutants, phase response light pulses
506 showed a much greater effect than the wild type, suggesting that clock resetting is light dependent
507 (Covington *et al.*, 2001), involving ELF3 in oscillator resetting by repressing the light input to the
508 clock (Bujdoso & Davis, 2013). However, the exact mechanism through which this occurs is
509 unknown.

510 *elf3* and *phyB* mutants were found to have similar phenotypic traits, such as hypocotyl
511 elongation in red light and constitutive shade avoidance (Devlin *et al.*, 1999). *elf3* mutants are also
512 defective in their response to blue and/ or red light with stronger effects showing in red light. ELF3
513 grown in darkness is rhythmic with a long-period phenotype, rhythmic in light/dark entrainment
514 cycles, but arrhythmic in free run light conditions (Hicks *et al.*, 1996). *elf3* plants are also unable to
515 inhibit hypocotyl elongation under light (Zagotta *et al.*, 1996). The combined phenotypic
516 characteristics of the *elf3* mutants suggest that ELF3 plays a role in light perception and signalling,
517 particularly in red light due to the interaction between ELF3 and phyB (Reed *et al.*, 2000).

518 *EARLY FLOWERING 4 (ELF4)* was the first clock component interpreted as being required for
519 the clock to cycle and it was revealed to be a component of normal light perception. Genetic loss of
520 *ELF4* resulted in plants that were markedly attenuated in the ability of a red-light pulse to generate
521 *CCA1* and *LHY* rhythms in etiolated plants. This was concluded to be due to ELF4 being required for
522 the phytochrome-mediated light induction of *CCA1* and *LHY* expression (Kikis *et al.*, 2005).
523 Consistent with this, it was shown that *elf4* mutants were hypermorphic and hypomorphic to red-
524 light cues, dependent on the assay. Notably, red-light mediated induction of *CAB2* expression was
525 elevated in *elf4* (McWatters *et al.*, 2007). This revealed that ELF4 contributes to so-called circadian
526 gating of light responsiveness (negative photomorphogenesis), light-regulation of *PIF4/5* expression
527 and the suppression of growth (positive photomorphogenesis) (Nozue *et al.*, 2007).

528 The presence of ELF4 in the nucleus increases the accumulation of ELF3 (Herrero *et al.*,
529 2012). ELF4 may function as a nuclear anchor for ELF3, but does not affect the nuclear localisation of
530 LUX, the third component of the evening complex (Herrero *et al.*, 2012). Nuclear import of phyB is
531 light dependent (Kircher *et al.*, 1999, Sakamoto & Nagatani, 1996), and it was shown that phyB does
532 not import ELF3 into the nucleus (Bujdoso & Davis, 2013). It is possible that ELF3 plays a role in the
533 nuclear import of phyB, as the N-terminus of ELF3 interacts with the C-terminal end of both the Pr
534 and Pfr forms of PHYB (Liu *et al.*, 2001). However, ELF3 and phyB have opposite roles in controlling
535 circadian oscillations (Herrero *et al.*, 2012). ELF3 needs the association with ELF4 to maintain
536 circadian oscillations, counteracting the COP1 and phyB mediated repression of ELF3 (Herrero *et al.*,
537 2012). ELF3 is also part of the blue-light signalling pathway, through its interaction with COP1. How

538 phyB and ELF4 coordinate the action and localisation of ELF3 seems critical for the cooperative
539 intersection of light perception and circadian clock function.

540 It was originally unclear what overall effect ELF3 has on other clock genes as the *elf3* loss of
541 function mutation causes arrhythmicity. A reduction-of-function mutation in *elf3-12* provided a way
542 to explore this, as the hypomorphic *elf3-12* allele is able to maintain rhythmicity (Kolmos *et al.*,
543 2011). This showed *elf3-12* to be light dependent but with a defective phase resetting mechanism.
544 This *elf3-12* mutant allowed the position of ELF3 within the clock to be derived as key to the
545 regulation of *PRR9* expression (Kolmos & Davis, 2007, Kolmos *et al.*, 2011). It is known that ELF3
546 associates to the promoter of *PRR9* to mediate its repression. In addition to clock-regulated *PRR9*
547 transcription, *PRR9* expression is also light regulated. Furthermore, *prp9* mutants display
548 photomorphogenic phenotypes (Nakamichi *et al.*, 2005). This highlights the role of ELF3 in
549 reciprocally linking light signalling to clock function.

550 Overexpression of *PHYA* in an *elf3-12* background showed that the overexpressed *PHYA* has
551 an additive effect with the *elf3-12* mutation to give a further shortened period in red light. In a range
552 of light conditions the *elf3-12 PHYA*-overexpression lines had an altered phase however in darkness
553 there was no change suggesting that light has an epistatic effect on *PHYA* (Kolmos *et al.*, 2011).
554 Overexpression of *PHYB* in the same *elf3-12* background gave the same period shortening as the
555 *PHYA*-overexpression lines; however the *PHYB-elf3-12* lines had a phase more closely linked to *PHYB*
556 overexpression in a wild-type background (Kolmos *et al.*, 2011). This result suggests that *PHYB*
557 functions upstream of *elf3-12* in light signalling and is able to suppress the effects of *elf3-12* (Bujdosó
558 & Davis, 2013). Together it appears that some, but not all, inputs of phytochromes to the clock
559 depend on ELF3.

560

561 Duration and quality of light

562 In regular light-dark cycles Arabidopsis has a circadian period of approximately 24 hours in
563 light, whereas in darkness it has a period of 30 to 36 hours (Millar *et al.*, 1995). Light therefore
564 makes the clock run faster, the absence of light cues causes the clock to slow, this is in keeping with
565 Aschoff's rule (Aschoff, 1979). The range of photoreceptors present in Arabidopsis allow a range of
566 fluence rates to be detected, ensuring the phase of the circadian oscillator is synchronised with
567 environmental cues (Somers *et al.*, 1998a), at both dawn and dusk (Devlin & Kay, 2000a). Removal or
568 even partial reduction of blue and red photoreceptors causes the clock to run slower (Millar *et al.*,
569 1995), suggesting that the effects of light intensity on the speed of the clock is limited by the number
570 of photoreceptors present. This would also suggest that it would not be possible to increase the
571 speed of the clock with higher light intensities beyond the maximum speed obtainable by that
572 number of photoreceptors.

573 Input of duration and quality of light are important in synchronising processes such as
574 flowering time and development (Weston *et al.*, 2000). Preceding photoperiod was shown to alter
575 the subsequent speed of the clock (Darrah *et al.*, 2006; Boikoglou *et al.* 2011). Interestingly here is
576 the long known role of ELF3 in processing light information to the clock (Hicks *et al.* 1996), and how
577 this coordinates the capacity for a plant to perceive daily boundaries present in a day night cycle
578 (McWatters *et al.* 2000). Recent work has revealed that extensive allelic variation at *ELF3* contribute
579 to alterations in photoperiodic control and this is associated to alterations in encoded nuclear
580 abundance and *in vivo* turn over diurnal time (Undurraga *et al.* 2012, Anwer *et al.* 2014). Combined
581 with temperature variation over the day, light duration gives information on the time of year or
582 season and therefore a warning of the growth conditions to follow. It is clear that allelic variation
583 exists in Arabidopsis to change the output of such varying entrainment processes (Darrah *et al.*,
584 2006, Boikoglou *et al.* 2011; Anwer *et al.* 2014).

585 Plants are able to adapt to changes in light intensity, such as consistently low light intensity,
586 by re-arranging photosynthetic machinery to be more efficient at light harvesting (Weston *et al.*,
587 2000). Blue light plays a major role in this. As such it would be assumed that cryptochromes and
588 *PHYA/B* play a role in directing the timing of light capture. A connection hub for this, COP1 has been

589 identified as a signalling intermediate between these two processes (Walters *et al.*, 1999), however
590 links between photoreceptor function and organisation of the photosynthetic apparatus await
591 further investigation (Walters *et al.*, 1999, Weston *et al.*, 2000). Finally light intensity is also detected
592 by the plastid sensing blue light, causing structural changes and elongation of the palisade to absorb
593 more light, this process responds a lot more to blue light than red (Weston *et al.*, 2000). It could be
594 hypothesised that this plastid information is used as a nuclear clock and is synchronised with the
595 phyA and phyB red light input to the central oscillator by COP1.

596

597 Discussion

598 Multiple photoreceptors are essential components of light input to the clock. In this way
599 they play a central role in the light input to the clock. Not only with the reversible, light-mediated
600 reactions for maximal efficiency in light or dimmer light / shade, they also directly input light into the
601 central oscillator through clock associated factors, such as ELF3/4, COP1, ZTL, PIFs, PILs and HFR.
602 Transcriptional regulation and post-translational processes are all part of this complex web of
603 interconnections between light-perception and clock function. Overall light input to the clock forms
604 complex feedback systems that generated harmonised regulatory pathways, the mechanisms from
605 light perception to clock function, and back again, awaits clear discoveries.

606 Many plant growth chambers are produced with red, blue and far-red LED panels, but are
607 these the optimal light regimes to measure plant gene expression under? Furthermore, most
608 chambers have a lights-on or off function which does not represent the graded changes in intensity
609 that would occur with a plant growing under natural sunlight (or in a greenhouse), with the gradual
610 appearance and disappearance of light at sunrise and sunset. As white light comprises a combination
611 of different wavelengths of light simultaneously, it may be possible that the pathways for different
612 colours of light interact more than has been found so far. Overlapping functions have been found
613 between blue and red light and these are the most commonly used light wavelengths for plant LEDs.
614 It is possible that there are essential components missing in just red and blue, although difficult to
615 isolate in a complex web of circadian gene expression, may only be present in white light or in other
616 light combinations not yet tested.

617 Light is essential for plant growth and it is therefore important to understand how plants
618 process the daily light cues they receive. Further understanding of how each light wavelength is
619 detected and the information fed into the central oscillator from each sensor, could potentially have
620 a large impact on plant and ultimately crop growth. With global changes in climate, knowledge on
621 essential lighting requirements and how this impacts on overall plant health could be used to
622 optimise crop productivity. Indoor farming techniques using LEDs as a light source could be
623 optimised for maximal yield and growth speed. As permafrost regions recede, and suitable growth
624 land becomes available. A detailed understanding of photoperiodicity and how it impacts fitness will
625 help with the challenges created by growing crops in shorter growth seasons and longer daylight
626 hours.

627

628 Figure legends

629

630 **Figure 1.** Schematic diagram of feedback loops in the Arabidopsis central oscillator.

631

632 **Figure 2.** Effects of light intensity on circadian period. A). Circadian gene expression is rhythmic in
633 constant light but in the absence of exogenous sucrose, rapidly becomes arrhythmic in prolonged
634 darkness. B). Following Aschoff's rule, high intensity light causes the clock to run faster; lower light
635 intensities cause the clock to slow. C). High light intensities result in period shortening; lower light
636 intensities result in period lengthening.

637

638 **Figure 3.** Circadian photoreceptors and their potential interactions to input light to the central
639 oscillator.

640

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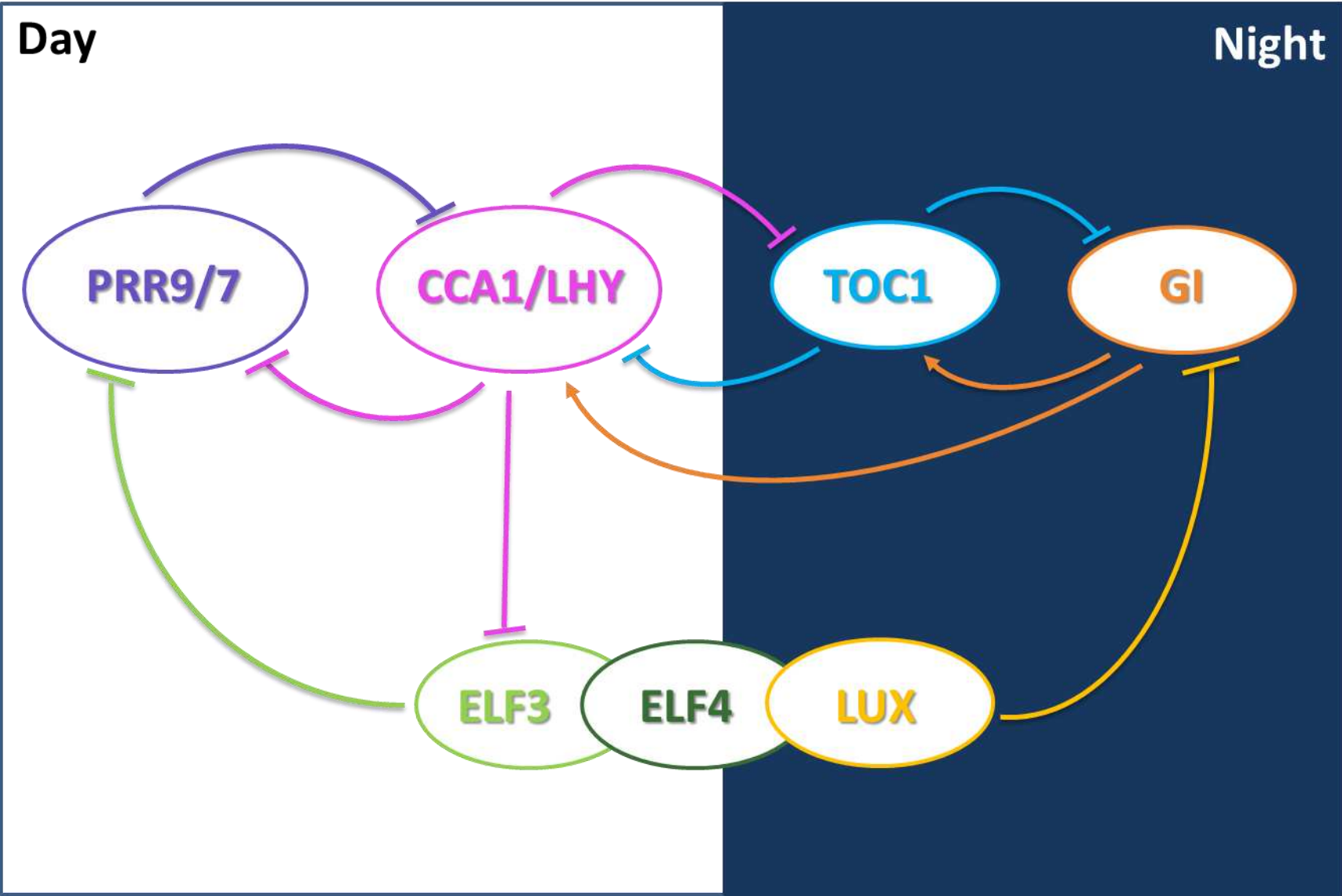
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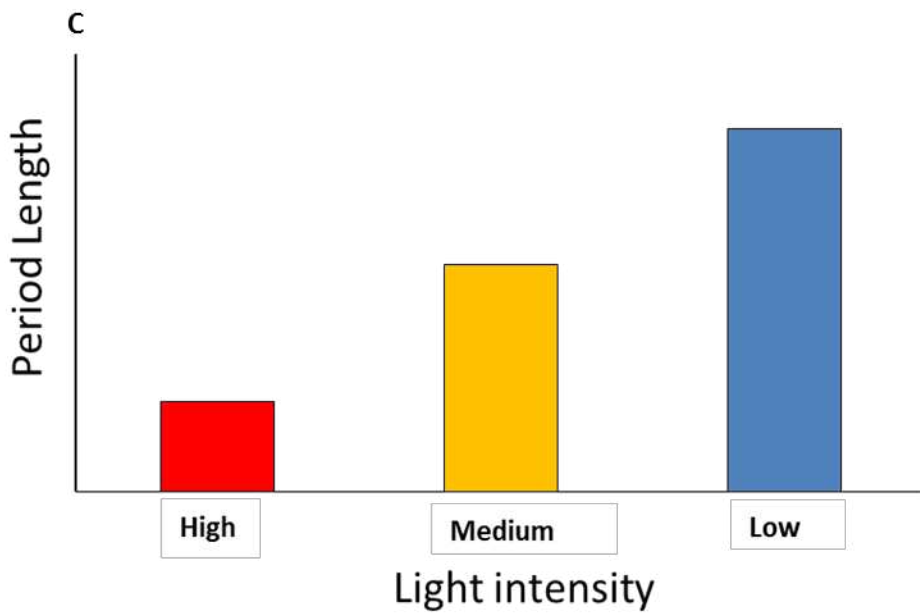
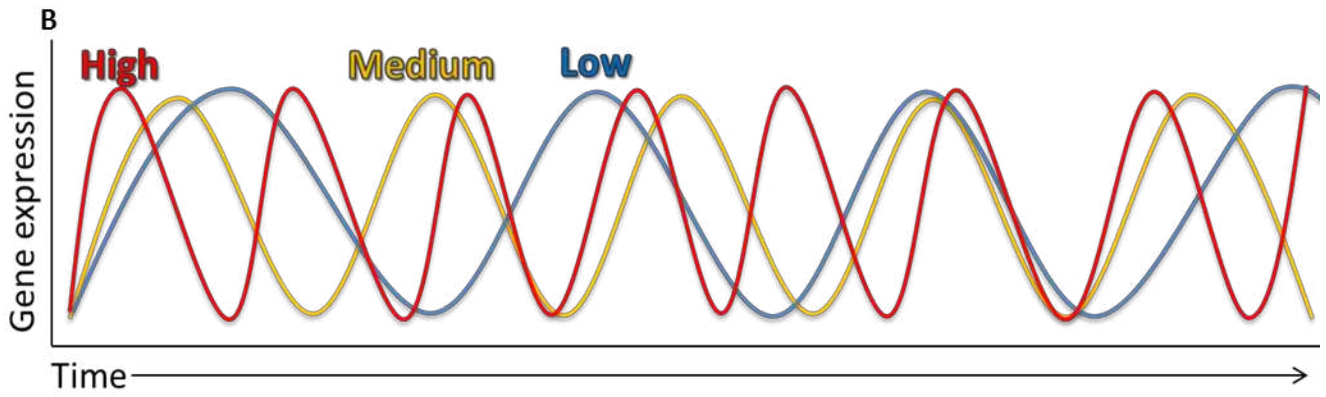
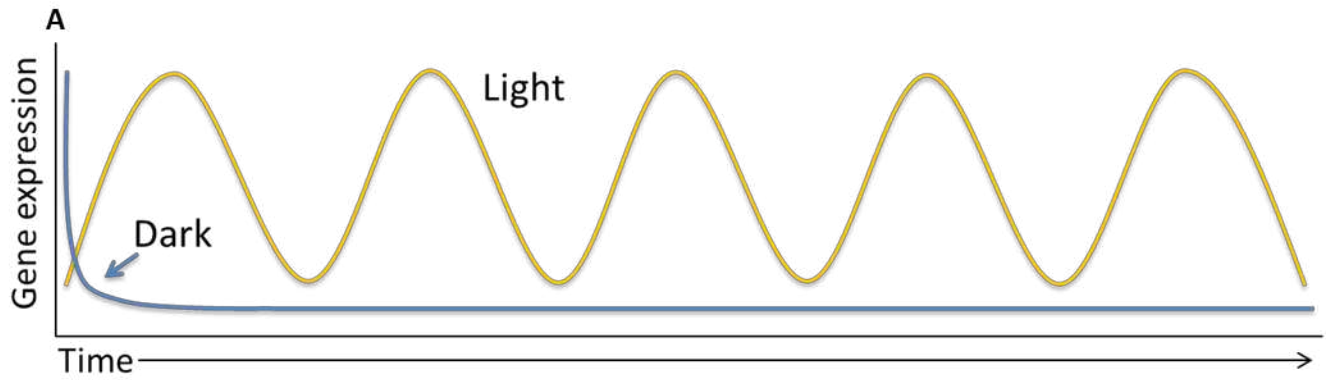
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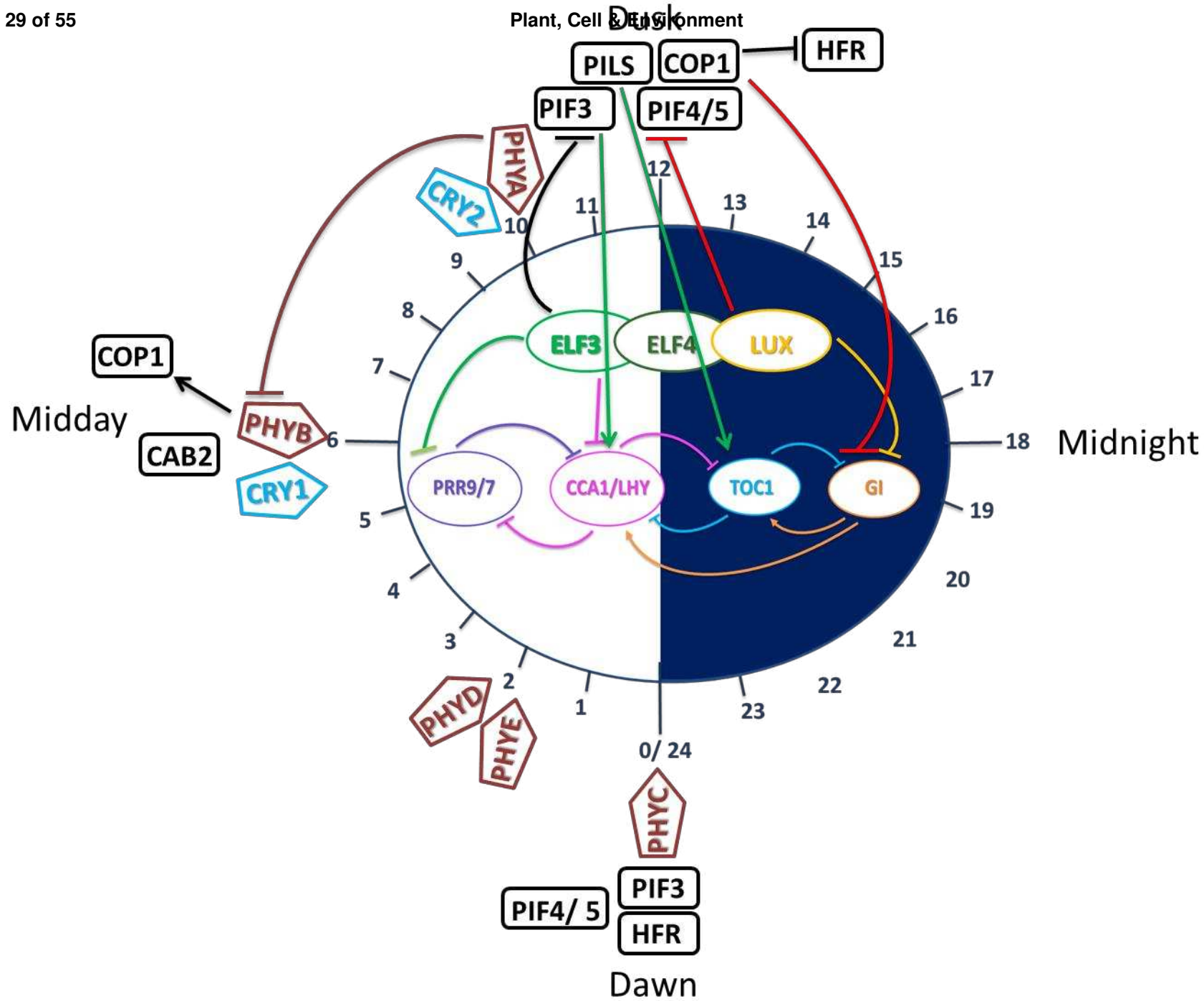
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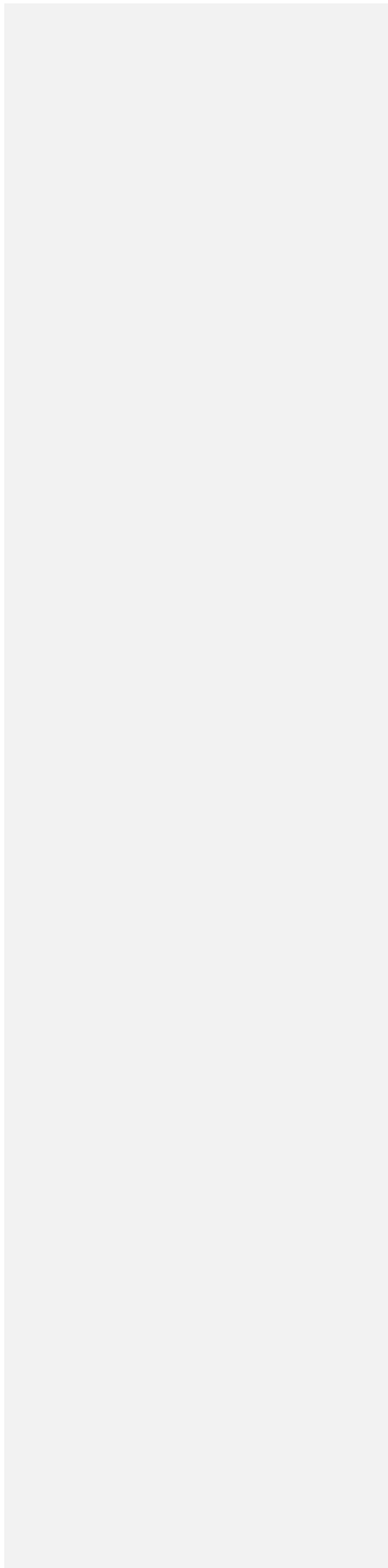






1 Shining a light on the Arabidopsis circadian clock
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For Review Only



14 Abstract

15

16 The circadian clock provides essential timing information to ensure optimal growth to prevailing
17 external environmental conditions. A major time-setting mechanism (*zeitgeber*) in clock
18 synchronisation is light. Differing light wavelengths, intensities and photoperiodic duration are
19 processed for the clock-setting mechanism. Many studies on ~~the~~ light-input pathways to the clock
20 have focused on *Arabidopsis thaliana*. Photoreceptors are specific chromic proteins that detect light
21 signals and transmit this information to the central circadian oscillator through a number of different
22 signalling mechanisms. The most ~~well-characterised~~ well characterised clock-mediating
23 photoreceptors are cryptochromes and phytochromes, detecting blue, red and far-red wavelengths
24 of light. Ultraviolet and shaded light ~~are also also are~~ processed signals to the oscillator. Notably, the
25 clock reciprocally generates rhythms of photoreceptor action leading to so-called gating of light
26 responses. ~~A number of~~ intermediate proteins, such as Phytochrome interacting factors (PIFs),
27 constitutive photomorphogenic 1 (COP1) and EARLY FLOWERING 3 (ELF3), have been established in
28 signalling pathways downstream of photoreceptor activation. However, the precise details for these
29 signalling mechanisms are not fully established. This review highlights both historical and recent
30 efforts made to understand overall light input to the oscillator, first looking at how each wavelength
31 of light is detected, this is then related to known input mechanisms and their interactions.

32

Review Only

33 The circadian clock

34 The circadian clock allows plants as sessile organisms to synchronise with diurnal changes in
35 the environment (Dodd *et al.*, 2005). Daily external environmental stimuli are required to initiate
36 circadian oscillations and to maintain synchronicity with the external environment. This process is
37 called entrainment. The environmental cues governing these processes are termed *zeitgebers* (from
38 German: "time givers"). The ability to synchronise with the external environment efficiently confers
39 enhanced fitness (Michael *et al.*, 2003).

40 Diurnal changes in cellular processes controlled by the clock allow plants to anticipate, and
41 therefore better survive, a range of stresses (Sanchez *et al.*, 2011). Diurnal changes have been
42 shown to occur in cold/freezing tolerance (Fornara *et al.*, 2015, Nakamichi *et al.*, 2009), drought
43 tolerance (Habte *et al.*, 2014), pathogen response (Shin *et al.*, 2012, Wang *et al.*, 2011) and
44 photosynthesis (Pyl *et al.*, 2012). This synchronisation is the product of a large number of
45 rhythmically regulated cellular processes (Bujdoso & Davis, 2013, Hanano *et al.*, 2008), many of
46 which are triggered by light perception (Wenden *et al.*, 2011). Perception of daily *zeitgebers*, such as
47 changes in light and temperature (Chow *et al.*, 2014, Harmer, 2009), enable plants to reset the clock
48 at dawn, and feed back to the central oscillator. For this light entrainment, photoreceptors play a
49 major role (Somers *et al.*, 1998a, Toth *et al.*, 2001). The circadian clock was derived from the
50 principle of inter-connected, positive and negative feedback loops (Shearman *et al.*, 2000). For the
51 purpose of this review, light input into the *Arabidopsis thaliana* (*Arabidopsis*) circadian clock will be
52 the focus of discussion, with a brief examination of clock components.

53 In *Arabidopsis*, morning expressed Myb-like transcription factors *CIRCADIAN CLOCK*
54 *ASSOCIATED 1* (*CCA1*) (Wang & Tobin, 1998) and *LATE ELONGATED HYPOCOTYL* (*LHY*) (Schaffer *et al.*,
55 1998) antagonize expression of the evening expressed pseudo-response regulator (PRR) *TIMING OF*
56 *CAB EXPRESSION 1* (*TOC1*) (Strayer *et al.*, 2000). These three genes form the core negative feedback
57 loop of the circadian oscillator (Alabadi *et al.*, 2001, Gendron *et al.*, 2012) (Figure 1). Several other
58 genes form additional loops within this core oscillator. In day time *CCA1* and *LHY* repress expression
59 of the pseudo-response regulators *PRR5*, *PRR7* and *PRR9* (Adams *et al.*, 2015, Kamioka *et al.*, 2016),
60 as well as *TOC1*, *GI*, and the genes that generate the evening complex (Locke *et al.*, 2006, Nakamichi
61 *et al.*, 2009, Pokhilko *et al.*, 2010, Zeilinger *et al.*, 2006). *GIGANTEA* (*GI*) is evening expressed and is
62 proposed to form an additional negative feedback-loop with *TOC1* (Locke *et al.*, 2006). All of these
63 loops are connected through the action of the evening complex formed by *LUX ARRHYTHMO* (*LUX*),
64 *EARLY FLOWERING 3* (*ELF3*) and *EARLY FLOWERING 4* (*ELF4*), which directly inhibits the expression of
65 *PRR9* (Helfer *et al.*, 2011, Herrero *et al.*, 2012), *PRR7*, *GI* and *LUX* (Mizuno *et al.*, 2014). The absence
66 of even one component of the evening complex gives rise to plants that are photoperiod insensitive.
67 This results in early flowering, long hypocotyl growth and arrhythmicity of the free-running circadian
68 period (Hazen *et al.*, 2005, McWatters *et al.*, 2007, Onai & Ishiura, 2005, Thines & Harmon, 2010).
69 The importance of the three evening-complex components is thusly highlighted in maintaining a
70 functional circadian clock, and therefore the physiological processes controlled by the clock, such as
71 the input of diurnal photoperiod information, (Covington *et al.*, 2001, Más *et al.*, 2003, Mizoguchi
72 *et al.*, 2005, Park *et al.*, 1999).

73

74 Effects of light on the clock

75 Light changes throughout a day-night cycle are pronounced and thus robustly entrain the
76 clock. In the light phase of a daily cycle, the dark to light transition of dawn is used as a time setting
77 checkpoint (Millar *et al.*, 1995). Prolonged darkness causes many of the core genes in the
78 *Arabidopsis* central oscillator to rapidly become arrhythmic, due to the lack of essential light time
79 setting cues (Figure 2a) (Millar *et al.*, 1995). This dampening effect, leading to arrhythmicity is
80 particularly noticeable in the absence of media containing sucrose. In prolonged darkness, sucrose
81 can act as a substitute for light in maintaining rhythmicity for a number of days (Bläsing *et al.*, 2005).
82 Light has two main modes to set the clock. The first is parametric entrainment; gradual entrainment
83 of the clock, such as the acceleration of the clock induced by increased light perception, which

84 eventually leads to a phase shift of the clock back to a correct resonance. Parametric entrainment
 85 follows Aschoff's rule, as light intensity increases, the speed of the clock increases. As intensity
 86 decreases, the speed of the clock slows (Aschoff, 1979), (Figure 2B/C). Increases in light intensity,
 87 lead to decreases in periodicity (Somers *et al.*, 1998a). The second light-induced time-setting
 88 mechanism is non-parametric entrainment: rapid re-entrainment. This leads to a rapid time setting
 89 of the clock at dawn (Millar & Kay, 1996). Non-parametric entrainment requires an extended light
 90 exposure far beyond that which activates light-regulated gene expression (Millar & Kay, 1996).
 91 Metabolic entrainment is also a mechanism for non-parametric entrainment (Haydon *et al.*, 2013,
 92 Sanchez-Villarreal *et al.*, 2013; Haydon & Webb, 2016; Shin *et al.*, 2017). The different
 93 photoreceptors and photochromic proteins involved in light entrainment are described in more
 94 detail below.

95

96 How are different wavelengths of light input to the *Arabidopsis* clock?

97 Diurnal organisms, particularly plants, are subjected to Aschoff's rule: an increase in light
 98 intensity accelerates the circadian-oscillator speed leading to shortening of periodicity (Aschoff,
 99 1979). Light input to the circadian clock is presumed to occur through the action of different types of
 100 photoreceptors (Somers *et al.*, 1998a). There are more than ten known circadian-associated
 101 photoreceptors (Edwards *et al.*, 2015). These can be split into four classes: phytochromes,
 102 cryptochromes, ZTL/FKF1/LKP2 family, and UVR8. Each receptor contributes in the dose-dependent
 103 perception of far-red, red, blue, and ultra-violet light (Cashmore *et al.*, 1999, Mas *et al.*, 2000, Rizzini
 104 *et al.*, 2011, Song *et al.*, 2012). It is presumed that the input of this information is co-ordinately
 105 relayed to the central oscillator.

106 Both phytochromes and cryptochromes play key roles in light responsive time setting
 107 mechanisms, in a manner that follows Aschoff's rule (Devlin & Kay, 2000a, Somers *et al.*, 1998a). This
 108 is due to the ability of both phytochromes and cryptochromes to form photoreceptor complexes
 109 (Más *et al.*, 2003) that are genetically interactive in clock function (Devlin & Kay, 2000a). Excitation
 110 of these photoreceptors cause the central oscillator to accelerate, changing the overall speed of the
 111 clock (Devlin & Kay, 2000b, Herrero *et al.*, 2012, Kolmos *et al.*, 2011, Somers *et al.*, 1998a, Somers
 112 *et al.*, 1998b). There are a number of different known mechanisms through which light absorption by
 113 photoreceptors input environmental information to the oscillator, however, these mechanistic
 114 details are not complete. Regulation of transcription by circadian gating restricts changes in RNA
 115 levels to specific times of day. Therefore preventing transcription of some light-regulated clock
 116 genes in response to unexpected external stimuli, for example light pulses during the night (Millar &
 117 Kay, 1996). Light regulation of myb transcription factors, such as *CCA1* and *LHY* effect the
 118 transcription and stability of other clock components, such as *PRR9/7* (Carre & Kay, 1995).
 119 Messengers such as Ca^{2+} and calmodulin signalling may also affect circadian regulation in response to
 120 light (Johnson *et al.*, 1995, Millar & Kay, 1996). Light also directly controls the degradation of *PRR5*,
 121 *PRR7*, *PRR9*, *TOC1* and *GI* proteins (David *et al.*, 2006, Farré and Kay, 2007, Ito *et al.*, 2007, Kiba *et*
 122 *al.*, 2007, Más *et al.*, 2003, Matsushika *et al.*, 2000). These degradation events then act on outputs
 123 within a diurnal context, which change in duration throughout the season (Davis, 2002, Guerriero *et*
 124 *al.*, 2012, Salazar *et al.*, 2009, Song *et al.*, 2012, Troein *et al.*, 2009). Light thus has multiple
 125 mechanistic inputs to clock processes, all of which control entrainment. How each individual
 126 wavelength of light is input to the clock will be discussed below.

127

128 Red light

129 Phytochromes are predominantly red-light photoreceptors, absorbing maximally at
 130 wavelengths between 600 and 700nm (Somers *et al.*, 1998a). *Arabidopsis* has five phytochromes
 131 (Sharrock & Quail, 1989), phyA-phyE (Mathews & Sharrock, 1997). Each phytochrome acts as a light
 132 input sensor to form regulatory feedback loops within the circadian clock. Phytochromes are in turn
 133 reported to be negatively regulated by the clock through cryptochrome (CRY) signals (Devlin & Kay,
 134 2000a, Mas *et al.*, 2000). Phytochromes exist in two interconvertible forms; the inactive Pr form is

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135 converted by red light to the active Pfr form which can be converted back to the inactive Pr state by
136 far-red light (Rudiger *et al.*, 1983). These conversion events between active and inactive forms of
137 phytochrome are essential to light input to the clock, as discussed below (see far red, PIFs, ELF3).
138 Each of the five phytochromes play distinct roles in light sensing.

139 phyA mediates entrainment responses to low intensity red light and pulses of light (Quail *et al.*
140 *et al.*, 1995, Somers *et al.*, 1998a). A *PHYA* deficiency mutation, results in an altered period length in
141 dim red light (Somers *et al.*, 1998a). It is not known how phyA signals to the clock as it has not been
142 reported to directly bind to a clock-associated factor, in contrast to the other four phytochromes
143 (Huang *et al.*, 2016).

144 phyB is the main detector for high intensity red light (Somers *et al.*, 1998a). Both phyB and
145 phyD are able to detect red and far-red wavelengths of light (Aukerman *et al.*, 1997, Devlin *et al.*,
146 1999). phyB physically interacts with ELF3 in the central oscillator to provide a direct light input to
147 the clock (Kolmos *et al.*, 2011, Liu *et al.*, 2001). *phyb* mutants show an altered response to shade
148 avoidance (Smith, 1995), which is also a phenotype of the *elf3* mutant (Huang *et al.*, 2016). phyC to
149 phyE also interact with ELF3 protein (Huang *et al.*, 2016), but this has not yet been connected to the
150 clock (Liu *et al.*, 2001). Under high fluence red light, *phyb* mutants and the phyB overexpressor have
151 a period defects and altered phase (Anderson *et al.*, 1997, Kolmos *et al.*, 2011, Salomé *et al.*, 2002,
152 Somers *et al.*, 1998a). Also altered cryptochrome signalling (see blue light below), phyB and CRY2
153 physically interact by translocating to the nucleus in red light (Mas *et al.*, 2000), where phyB is then
154 suppressed by CRY2 (Mas *et al.*, 2000). This alters clock performance under white light conditions (red
155 and blue light together) (Devlin & Kay, 2000a).

156 In non-peer-reviewed work, phyC was found to play a role in white-light input and red-light
157 detection. Mutations in *PHYC* result in a long-period phenotype, which was shown to be
158 temperature dependant, suggesting that phyC inputs not only light information to the clock, but also
159 temperature (Edwards *et al.*, 2015, Franklin *et al.*, 2003, Qin *et al.*, 1997). phyE along with phyD plays
160 a role in controlling the period length of *CAB* gene expression, however, many of the clock effects of
161 phyE and phyD are masked by phyB (Franklin & Quail, 2010). phyE works with phyB and phyD in the
162 regulation of shade avoidance (Devlin *et al.*, 1998). Interestingly, the promoters of *PHYA* and *PHYB*
163 are down-regulated by light, whereas the *PHYC* promoter is upregulated (Tóth *et al.*, 2001), *PHYD*
164 and *PHYE* do not show changes in expression in response to light changes. *PHYB,D,E* mediate high
165 fluence red light input to the clock with *PHYA,B,D,E* acting additively to input red-light information to
166 the clock, as a result the clock runs faster as the detected intensity of red light increases (Devlin &
167 Kay, 2000a). The absence of all five phytochromes results in severally attenuated rhythms, but not a
168 total loss of clock function (Hu *et al.*, 2013). Together, all five phytochromes play differing roles in
169 mediating light-dependant changes in periodicity.

170

171 Blue light

172 Cryptochromes are blue light (492 to 455nm) and UVA photoreceptors present in both
173 plants and animals (Cashmore *et al.*, 1999). The *HY4* locus was found to encode cryptochrome 1
174 (CRY1). It was identified due to *cry1* (*hy4*) mutants growing with a long-hypocotyl phenotype and
175 being unable to respond to blue light (Ahmad & Cashmore, 1993, Koornneef *et al.*, 1980), *cry1/hy4*
176 plants are also late flowering (Goto *et al.*, 1991, Millar *et al.*, 1995). *cry1* mutants have a long period
177 under blue light (Somers *et al.*, 1998a), suggesting CRY1 acts as a photoreceptor for blue-light
178 entrainment of the clock (Devlin & Kay, 2000a). Overexpression of *CRY1* caused increased sensitivity
179 to blue light and period shortening (Lin *et al.*, 1996, Somers *et al.*, 1998a). CRY1 is a soluble protein
180 when grown in both light and dark conditions in *Arabidopsis* (Lin *et al.*, 1996), CRY1 is more stable
181 than CRY2 and works at higher light intensities (Lin *et al.*, 1998). Cryptochrome 2 (CRY2) can detect
182 low intensity light and is rapidly degraded under blue light (Lin *et al.*, 1998). In light, *CRY2* promoter
183 activity is down-regulated whereas, *CRY1* is upregulated (Tóth *et al.*, 2001). The *cry2* mutation alters
184 sensitivity to photoperiod and flowering in *Arabidopsis*, but does not have a detectable individual
185 effect on circadian rhythm (Devlin & Kay, 2000a, Guo *et al.*, 1998). Overexpression of either *CRY1* or

186 CRY2 gives rise to a higher blue-light sensitivity under low light conditions than in the individual
 187 overexpression lines (Ahmad *et al.*, 1998a). Double mutant *cry1, cry2* plants are rhythmic, suggesting
 188 that although CRY1 inputs blue light into the clock CRY1 and 2 are not part of the central oscillator
 189 (Devlin & Kay, 2000a). However, CRY1 and CRY2 gene expression oscillates with a circadian rhythm
 190 under constant light (Harmer *et al.*, 2000). CRY1 and 2 work together to input information to the
 191 clock in a similar way to phyA and B, but at differing light intensities.

192 Phytochromes are able to absorb low fluence blue light alongside CRY1 for period length
 193 control. *phyA* mutants show a period lengthening effect when free run under blue light (Somers *et al.*,
 194 1998a). Without phyA detection of blue light, the input relies on CRY1 alone causing the period
 195 to lengthen as the plant detects less light than the actual ambient intensity of irradiation.
 196 Conversely, *PHYA* overexpression has been proposed to cause period shortening under blue light, as
 197 more blue light is processed as an input than the actual ambient light intensity. Phytochromes thus
 198 also work in blue-light signalling to the clock.

199

200 High light synergism - (White light)

201 White light comprises of multiple light wavelengths. As such, interactions between
 202 phytochromes and cryptochromes are needed to input this information into the circadian clock.
 203 These interactions were found with loss of function mutants for both phytochromes and
 204 cryptochromes. In wild-type plants *CAB2* period decreases as light intensity increases, *cry2* mutants
 205 were found to be deficient in a white light response as they have a *CAB2* period increase in response
 206 to high light (Mas *et al.*, 2000). This period increase was not detected in either red or blue light
 207 alone, suggesting that to be active CRY2 needs multiple wavelengths of light simultaneously and
 208 phyB (Mas *et al.*, 2000). CRY1 was also found to be required for phyA signalling as *cryCRY1* and
 209 *cryCRY2* mutants are unable to detect red light above the fluence range of both phyA and phyB
 210 (Devlin & Kay, 2000a). Light induces nuclear compartmentalisation of phytochromes where phyA
 211 and phyB directly interact with CRY1 and CRY2 (Mas *et al.*, 2000), the kinase activity of phyA
 212 phosphorylates CRY1 and CRY2 (Ahmad *et al.*, 1998b).

213 Phytochromes and cryptochromes facilitate signal integration of multiple light cues. CRY2 is
 214 activated when illuminated by multiple wavelengths of light suggesting it is needed for phytochrome
 215 activation (Mas *et al.*, 2000). This is also highlighted as both cryptochromes reach peak RNA
 216 expression with a similar expression pattern to the corresponding phytochromes (Toth *et al.*, 2001).
 217 It was found that the active Pfr form of phytochrome is needed for CRY2 expression, CRY2 then
 218 suppresses *PHYB* expression. However, PfrB is able to override CRY2 signalling to flowering time
 219 control via pathways, such as COP1 (see below). PfrB binding to the intermediate SPA1 allows
 220 degradation of the COP1-SPA1 complex, which is needed as an intermediate of CRY1/2 induced
 221 inhibition of photomorphogenic factors such as HFR and CO (Mas *et al.*, 2000, Sheerin *et al.*, 2015).
 222 Additionally, both CRY1 and CRY2 were found to be phosphorylated by the kinase activity of phyA
 223 (Ahmad *et al.*, 1998b; Mas *et al.*, 2000). It could be considered that phytochromes and cryptochromes
 224 work together in the "white light" response, which is a more than the additive effect of plants grown
 225 under blue and red light. However, quadruple mutants for *phyA, phyB, cry1* and *cry2* still showed
 226 rhythmic leaf movement in response to light-dark cycles suggesting that other photoreceptors must
 227 play a role in overall light input to the circadian clock (Yanovsky *et al.*, 2000). However, the exact
 228 relationship between phytochromes and cryptochromes is yet to be resolved.

229

230 ZTL family; blue-light absorbing with action under red-light and darkness

231 Zeitlupe (ZTL), also reported as ADAGIO1 (ADO1), links light input by both cryptochromes
 232 and phytochromes to the clock (Jarillo *et al.*, 2001, Kim *et al.*, 2007). *ZTL* mutant lines showed
 233 altered cotyledon movement and gene expression under different light conditions (Jarillo *et al.*,
 234 2001). Under blue and white light, *ztl* plants have a long period whereas under red light the *ztl* lines
 235 were reported to be arrhythmic for *CCR2* expression, cotyledon movement and stem elongation
 236 (Jarillo *et al.*, 2001). *ZTL* mutants were found to have a long-period phenotype for *CAB/TOC1* under

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237 red light (Kevei *et al.*, 2006, Kim *et al.*, 2005). ZTL thus is required for the perception of multiple
238 wavelengths of light into the oscillator.

239 ZTL encodes a protein reported to be a blue-light photoreceptor, as it contains a PAS
240 domain, F box domain linking proteins to a SCF ubiquitination complex, kelch repeats and a light,
241 oxygen or voltage (LOV) domain allowing protein-protein interactions (Mas *et al.*, 2003). Interactions
242 between TOC1 and ZTL were found to occur through these kelch-repeat zones (Kevei *et al.*, 2006).
243 The PAS/ LOV domain were identified as essential for coupling ZTL to red light (Kevei *et al.*, 2006),
244 which was then found to occur through ZTL binding to the C-terminus of PhyB and CRY1 (Kim *et al.*,
245 2007).

246 ZTL is constitutively expressed at the RNA level, however, oscillations in ZTL protein levels
247 are seen (Kim *et al.*, 2007). These are proposed to result from the binding of Gigantea (GI) to
248 maintain the stability of ZTL. ZTL protein folding is chaperoned by HSP90 (Kim *et al.*, 2011), GI binds
249 to the ZTL-HSP90 complex to ensure specificity of protein folding (Cha *et al.*, 2017, Kim *et al.*, 2011).
250 interactions between ZTL and GI are enhanced by blue light through the LOV domain in ZTL (Kim *et al.*
251 *et al.*, 2007). ZTL controls proteasomal degradation of TOC1 (Más *et al.*, 2003). This ZTL-GI interaction
252 is believed to control a central part of the circadian oscillator. ZTL and ELF3 were reported to have
253 opposite effects on clock function. *ztl* mutants and *ELF3* overexpression lines show a lengthened
254 circadian period in light. Conversely *elf3* mutants and ZTL overexpression lines are reported as
255 arrhythmic under constant light (LL) (Kim *et al.*, 2005). However, the *elf3-ztl* double mutant showed
256 that ELF3 and ZTL have additive effects on the clock (Kim *et al.*, 2005). As GI controls the HSP90
257 mediated stabilisation of ZTL protein (Cha *et al.*, 2017, Kim *et al.*, 2011), ZTL protein then causes
258 protein depletion of TOC1 via ubiquitination (Kim *et al.*, 2011). ELF3 interacts as a substrate adaptor
259 for COP1 (an E3 ubiquitin ligase) to bind to and degrade GI protein, as a light input signal and
260 indicator of day length in response to CRY2 (Yu *et al.*, 2008). The reduction of GI then prevents the
261 formation of stable ZTL protein. ~~Therefore consequently preventing this prevents~~ ZTL-mediated
262 inhibition of TOC1 in the central oscillator, and ~~facilitating facilitates~~ TOC1 action. ~~ZTL also negatively~~
263 ~~regulates PRR5 by targeting PRR5 protein for degradation by via the 26S proteasome (Fujiwara et~~
264 ~~al., 2008, Kiba et al., 2007). As PRR5 forms a negative regulatory feedback loop with LHY/ CCA1, ZTL~~
265 ~~also therefore indirectly plays a role in the regulation of LHY/CCA1 within the central oscillator~~
266 ~~(Baudry et al., 2010). The relationship of ZTL to other clock components is yet to be established.~~

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267 Far-red light

268 *phyA* is the presumed photoreceptor for detecting monochromatic far-red light. Mutations
269 in *PHYA* resulted in loss of capacity for clock function (Wenden *et al.*, 2011). ELF4 was proposed to
270 restrict far-red perception in those studies. Interestingly, the active form of *phyA* (*phyA-Pfr*) is
271 formed under far-red light (Clough & Vierstra, 1997), given that far red converts the Pfr form of
272 phytochrome back to the inactive Pr form. In part perhaps *phyA* evolved the ability to form Pfr under
273 far red as a response to the change in light quality at the end of the day, which signals the transition
274 from day to night and therefore the associated changes in environment. However, far red can also
275 be a signal of shade due to far red being one of the only wavelengths of light able to pass through
276 leaves (Federer & Tanner, 1966), suggesting that there may be different mechanisms to entrain the
277 clock in these two different circumstances, as described in the next section. Plants in constant far-
278 red light have a faster clock and show high expression of evening genes, such as *PRR1/TOC1*, and low
279 expression of the morning genes *CCA1* and *LHY* (Wenden *et al.*, 2011). The exact mechanism of far-
280 red input to the clock is not fully characterised. However, far red has been shown to be involved in
281 the prevention of the interaction between Pfr and PIF3 (Martínez-García *et al.*, 2000). ELF4 was
282 identified as playing a role in mediating far-red light input to the clock (Wenden *et al.*, 2011), Far-red
283 light was used to aid recovery of rhythmicity in the otherwise arrhythmic *elf3* and *elf4* mutants
284 (Kolmos *et al.*, 2011, Wenden *et al.*, 2011).
285
286

287 Shaded light

288 White light with supplementary far-red light causes the clock to slow down (Jiménez-Gómez
289 *et al.*, 2010). Under shade, far red and potentially green light are present; there is a large overlap
290 between far-red signalling and shade. Shade however, is a useful environmental indicator to plants
291 for neighbour detection. *phyA* is thought to have the most involvement in mediating far-red
292 signalling, but *phyB* also plays a key role (Kolmos *et al.*, 2011, Wenden *et al.*, 2011). Shading plants
293 during the afternoon was found to have the greatest effect (Sellaro *et al.*, 2012). Responses to shade
294 involve the degradation of phytochrome interacting factors, namely PIF4 and 5 (Lorrain *et al.*, 2008).
295 PRR5 was found to regulate the shade-avoidance response by controlling PIF4 and PIF5, as well as
296 downstream components of the phytochrome-mediated signalling pathway. Furthermore ZTL
297 induces degradation of PRR5. However, this degradation was found to be repressed under blue light.
298 It was suggested that PRR5 gates phytochrome mediated shade responses (Takase *et al.*, 2013). *ELF3*
299 and *LUX* mutants (both components of the evening complex) show a reduced response to all
300 wavelengths of light therefore growing with elongated hypocotyls as though under shade (Jiménez-
301 Gómez *et al.*, 2010, Sellaro *et al.*, 2012, Zagotta *et al.*, 1996). This implies that *ELF3* and the evening-
302 complex also play a role in the shade response to the clock (Kolmos *et al.*, 2011).

303 UV-B light

304 Ultraviolet B light (UVB) can be one of the more damaging wavelengths present in sunlight.
305 UVB is a wavelength that is easily absorbed and damages both DNA and proteins (Jansen *et al.*,
306 1998), thus making UVB a useful light signal, but at the cost of inducing a stress response. UVB is an
307 "anti-shade" signal informing a plant it is under direct sunlight. At lower-fluence rates, UV-B light is
308 able to control development, promote photomorphogenesis, and drive gene expression (Heijde &
309 Ulm, 2012). *Ultraviolet resistance locus 8 (UVR8)* drives signalling for the majority of UVB responses
310 (Favory *et al.*, 2009, Rizzini *et al.*, 2011). Under UVB light, COP1 promotes the induction of elongated
311 hypocotyl 5 (HY5) and HY5 homologue (HYH) which induce stress responses such as flavonoid
312 biosynthesis to reduce UVB induced damage (Stracke *et al.*, 2010). UVR8 and COP1 are also crucial
313 for UVB light entrainment of the clock (Fehér *et al.*, 2011). Under white light supplemented with UV-
314 B light, COP1 induces HY5 and HYH, HY5 and HYH have not yet been implicated for clock
315 entrainment by UVB (Fehér *et al.*, 2011). UVR8 is able to mediate both parametric and non-
316 parametric entrainment, by inducing *PRR9* and *GI* under continuous light, alongside an increase in
317 *CCA1* and *ELF3* response to UVB light pulses. UVR8 was identified as the UVB receptor that can
318 mediate signal input to the oscillator, due to the fact that *uvr8* plants cannot input UVB light into the
319 oscillator, (Fehér *et al.*, 2011, Heijde & Ulm, 2012). It has been proposed that UVR8 mediates UVB
320 light input into the central oscillator by inhibiting PIF4 in the presence of UVB light. This requires
321 COP1-mediated repression of *PIF4* transcript, and also through the stabilisation of HFR, which
322 inhibits PIF4 (Hayes *et al.*, 2017). Canonical pathways used in UVB signalling mediate entrainment in
323 the clock, but the critical nodes in entrainment are not fully resolved.-(Hayes *et al.*, 2017).

324 Green light

325 Many studies have been carried out to test the physiological effects that occur as a
326 consequence of increased or absent green-light wavelengths. The mechanisms of sensing and input
327 to the circadian clock are yet to be understood. It is thought that green wavelengths can operate via
328 both a cryptochrome dependant and independent pathway (Folta & Maruhnich, 2007). Green light
329 can reverse the effect of blue light on hypocotyl elongation (Bouly *et al.*, 2007, Folta, 2004),
330 potentially due to the reversal of the blue light degradation of CRY1 (Bouly *et al.*, 2007). This could
331 then have an effect on photoperiod and subsequently flowering time (Banerjee *et al.*, 2007, Folta &
332 Maruhnich, 2007). The association of green light to cryptochromes was also shown by (Lin *et al.*,
333 1996) as overexpression of CRY1 causes increased sensitivity to green light. A reversible interaction
334 between CRY and green light similar to that found for phytochrome in red and far red light suggests
335
336

337 that there are intermediate signalling factors similar to PIFs that are yet to be identified. It is thus
338 plausible that green light could entrain the clock, but no definitive experiments have tested this.

339 Transcriptional regulation of photoreceptors by the clock.

340
341
342
343 The circadian clock generates rhythms of RNA and/or accumulation for all photoreceptor
344 classes. Starting with the discovery that *phyB* mRNA is rhythmic (Bognár *et al.*, 1999, Toth *et al.*,
345 2001, Tóth *et al.*, 2001), subsequent findings revealed that all five phytochromes in Arabidopsis
346 cycle. Interestingly, sub-nuclear accumulation of phytochrome holoprotein also appears to be under
347 clock control. However, the implications of this are currently unclear. Similarly, *CRY* genes are
348 rhythmic (Toth *et al.*, 2001). For UVR8, as UV light induces dimer disassembly to a monomer state, a
349 diel cycle of dimers at night and monomers during the day occur (Findlay & Jenkins, 2016). *UVR8*
350 mRNA displays robust circadian rhythms with a peak around subjective dusk (Mockler *et al.*, 2007).
351 For ZTL, the mRNA generated does not cycle, but robust protein cycling is readily detectable.
352 Together it is clear light receptors that act as input components to the clock, are themselves
353 circadian-output regulated.

354 Phytochrome input to the central oscillator

355
356 Light input to the central oscillator is a daily *zeitgeber*, but the central oscillator also acts as a
357 feedback mechanism to phytochromes over the day. The oscillator receives a number of light queues
358 during the light phase of each day from photoreceptors detecting the different ratio of light
359 wavelengths across the day. In turn, the oscillator inhibits expression of phytochrome proteins at
360 points hypothesised in Figure 3.

361 At dawn (ZT0), *PHYC* peaks with the return of light and changing temperature (Toth *et al.*,
362 2001). HFR increases due to increased stability (Yang *et al.*, 2005). PIF4/5 expression peaks at dawn
363 (Nomoto *et al.*, 2012), due to the lack of phytochromes, thus preventing phytochrome-induced
364 degradation at dawn (Shin *et al.*, 2013). PIF4/5 continue to be present throughout the light phase,
365 but are slowly degraded by interactions with the Pr form of phytochrome, PIFs can also interact with
366 LHY, CCA1. PfrB interacts with PIF3, where PIF3 then binds to the G-box domain of *CCA1/LHY*
367 promoters. CCA1 and LHY, as MYB transcription factors, then control other genes within the central
368 oscillator, such as *PRR5*, 7 and 9, as well as non-circadian genes (Martínez-García *et al.*, 2000, Wang
369 & Tobin, 1998).

370 *PHYD* and *E* are expressed two hours after dawn (Toth *et al.*, 2001). During the first half of
371 the light phase (ZT0-6) there is an increase in light intensity up to ZT6, and alongside this, an
372 increasing expression of phytochromes. *PHYB* and *CRY1* reach peaks in expression around mid-day
373 (ZT6) as both *phyB* and *CRY1* work at high-light intensities (Lin *et al.*, 1996, Lin *et al.*, 1998, Toth
374 *et al.*, 2001). *CAB1* expression peaks around mid-day as does the expression of HFR (Yang *et al.*, 2005).
375 HFR is thought to interact with PIF3 (Fairchild *et al.*, 2000), but the mechanism through which this
376 happens is not fully understood.

377 Both *PHYA* and *CRY2* peak towards the latter half of the light phase (ZT6-12) with the
378 decreasing light and increasing far red intensity (Toth *et al.*, 2001). *CRY2* detects lower intensity light
379 (Lin *et al.*, 1998), and the Pfr form of phytochrome is needed for *CRY2* activation (Mas *et al.*, 2000).
380 *CRY2* then suppresses *PHYB* expression (Mas *et al.*, 2000). *phyA* is essential in controlling the clock in
381 low light (Quail *et al.*, 1995, Somers *et al.*, 1998a) and far red conditions (Wenden *et al.*, 2011),
382 potentially through the Pfr form of phytochrome being unable to interact with PIF3 (Martínez-García
383 *et al.*, 2000).

384 At dusk, *CAB2* expression decreases, and *COP1* expression increases (Yang *et al.*, 2005),
385 allowing *COP1* suppression of HFR throughout the dark phase of the day. *COP1* accumulation along
386 with *ELF3* inhibits *GI* late in the afternoon (Yu *et al.*, 2008). PILs are rapidly produced during the first
387 hour of shade, early into the dark phase and work with *TOC1* to restrict growth (Salter *et al.*, 2003).

388 PIF3 is at its highest level at dusk due to its interactions with the Pfr form of phytochrome and the
389 highest level of Pfr being present just before dusk. Allowing information on high levels of far red light
390 to be input to the central oscillator (Martínez-García *et al.*, 2000). The evening complex (ELF3, ELF4,
391 LUX) inhibits the transcription of *PIF4/5* at dusk (Herrero *et al.*, 2012, Nusinow *et al.*, 2011; Raschke
392 *et al.* 2015). This allows PIF protein to accumulate stably due to the lack of phytochrome inhibition
393 overnight, which thus promotes growth, reaching a maximal level at dawn (Shin *et al.*, 2013, Delker
394 *et al.* 2014; Raschke *et al.* 2015).

395

396 COP1

397 Constitutive photomorphogenic 1 (COP1) is an E3 ubiquitin ligase, mediating day length
398 input to the clock and flowering time. COP1 is negatively regulated by a direct protein-protein
399 interaction with CRYs (Jang *et al.*, 2008, Wang *et al.*, 2001, Yang *et al.*, 2000). *phyA* and *B* affect the
400 nuclear abundance of COP1 (Osterlund *et al.*, 1999), as the C-terminal domain of *phyB* directly
401 interacts with COP1 (Millar *et al.*, 1994). COP1 acts as an intermediate, inputting photoperiodic
402 information from PHY and CRY into the oscillator. COP1 in turn plays a negative regulatory role
403 targeting *phyA*, *phyB* and *HFR1* for ubiquitination (Osterlund *et al.*, 2000, Seo *et al.*, 2003, Yang *et al.*,
404 2005).

405 CRY1, CRY2, *phyA* and *phyB* all interact with COP1 via Suppressor of Phytochrome A (SPA).
406 SPA1 is a nuclear localised repressor of phytochrome signalling (Hoecker *et al.*, 1999), which
407 interacts with COP1 (Hoecker & Quail, 2001). SPA1 contains a coiled-coil domain that enhances the
408 E3 ligase activity of COP1 on its targets (Seo *et al.*, 2003). The interactions between the 4 known SPA
409 proteins and COP1, negatively regulate light signalling in response to certain wavelengths of light
410 (Laubinger *et al.*, 2004, Zhu *et al.*, 2008). COP1-SPA1 interaction is repressed by activated CRY1 in
411 blue light (Lian *et al.*, 2011), CRY2 interacts with COP1 via SPA1 to allow COP1 proteolysis of CO to
412 control flowering time under blue light (Zuo *et al.*, 2011). The CRY1-SPA1 interaction enhances CRY2-
413 SPA1 activity in response to blue light to suppress COP1 activity resulting in a suppression of CO
414 degradation (Ordoñez-Herrera *et al.*, 2015, Zuo *et al.*, 2011).

415 In seedlings, *phyA* binds to SPA1 and 2 whereas, in adult plants *phyA* binds to SPA3 and 4
416 (Laubinger *et al.*, 2004). Binding of *phyB* to SPA1 is Pfr dependant allowing degradation of
417 COP1/SPA1 in light conditions that promote nuclear accumulation of *phyA* and *B*, this enhances light
418 responses, as the disruption of COP1/SPA1 interaction prevents degradation of photomorphogenic
419 factors such as *HFR*, and *HY5* (Sheerin *et al.*, 2015). The COP1/SPA complex is an important factor in
420 repression of light responses in darkness, as the COP1/SPA complex interacts directly with
421 photoreceptors leading to its inactivation (Huang *et al.*, 2014).

422 Within the central oscillator, COP1 interacts with ELF3 to mediate COP1 degradation of GI
423 late in the afternoon (Yu *et al.*, 2008), potentially using ELF3 as an adaptor for COP1 binding to GI
424 (Liu *et al.*, 2008). It is also possible that COP1 regulates the level of ELF3 present, in *cop1* mutants
425 ELF3 protein accumulates to higher levels than in the wild type, but the mRNA levels remain
426 unchanged (Liu *et al.*, 2001). [The result](#)

427 COP1 is also involved in UVB signalling as *cop1* mutants are deficient in a UVB response
428 (Oravec *et al.*, 2006). In the early stage of UVB signalling, UVR8 and COP1 directly interact in the
429 nucleus (Favory *et al.*, 2009), UVR8 and COP1 were found to be essential for UVB entrainment (Fehér
430 *et al.*, 2011). *HY5* and *HYH* which are also important components of UVB signalling are regulated by
431 COP1 (Brown & Jenkins, 2008). In the light COP1 detaches from *HY5* allowing stabilisation and the
432 light responsive target genes of *HY5* to be activated (Yi & Deng, 2005). COP1 plays an important
433 mediator role in the input of light from photoreceptors to the oscillator. In turn its regulation is
434 dependent on photoreceptors, the short-period phenotype in mutant lines shows that COP1 plays a
435 negative regulatory role on the clock.

436

437 PIFs and PILs

438 Phytochrome interacting factors (PIF) are a family of basic helix loop helix transcription
439 factors. There are 4 well characterised PIFs, PIF1,3,4,5 (Leivar *et al.*, 2012). (Pfeiffer *et al.*, 2012) PIFs
440 are unstable in the light due to their interaction with active phytochrome causing phosphorylation
441 and subsequent degradation (Leivar *et al.*, 2012, Soy *et al.*, 2012). The most well characterised PIF is
442 PIF3, which was found to interact with the Pfr form of phytochrome B (PfrB) acting as a bridge
443 between PfrB and its target gene by translocating PfrB to the nucleus. Thus allowing light induced
444 control of gene expression, as PIF3 does not interact with the Pr form of phytochrome (Martínez-
445 García *et al.*, 2000, Pfeiffer *et al.*, 2012). PIFs are also able to input information to the clock via direct
446 interaction with clock genes that contain a G-box motif in their promoter, PIFs can interact directly
447 with *LHY*, *CCA1*, *PRR5*, *PRR7*, *PRR9* and *LUX* (Martínez-García *et al.*, 2000). This is potentially one of
448 the main mechanisms through which light/ day length information is used to control or alter the
449 clock. [The central oscillator in turn regulates PIF expression. Postdusk, TOC1 peaks in expression, allowing direct interactions between TOC1 and PIF3, which results in the TOC1 gating of PIF induced growth, until TOC1 levels decrease predawn \(Soy *et al.*, 2016\).](#)

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452 *PIF4* and 5 show rhythmic expression with a diurnal peak at dawn (Nomoto *et al.*, 2012).
453 Expression of *PIF4* and 5 is controlled by the evening complex, comprising of ELF3, ELF4 and LUX
454 (Herrero *et al.*, 2012), which binds to the promoter region of *PIF4* and 5 to inhibit transcription at
455 dusk (Nusinow *et al.*, 2011). PIF protein stably accumulates overnight due to the lack of
456 phytochrome induced degradation to reach their maximum level at dawn (Shin *et al.*, 2013). As PIFs
457 are growth-promoting factors (Shin *et al.*, 2013), this leads to the highest growth rate occurring at
458 the end of the night phase.

459 PIFs may also input information from other environmental cues to the clock such as
460 temperature (McClung & Davis, 2010; Raschke *et al.* 2015). It was shown that *PIF4* expression also
461 increases in response to temperature increases (Shin *et al.*, 2013). As dawn induces a temperature
462 increase, alongside the return of daylight it would perhaps be advantageous to a plant to be able to
463 input both of these environmental cues into the clock at the same time.

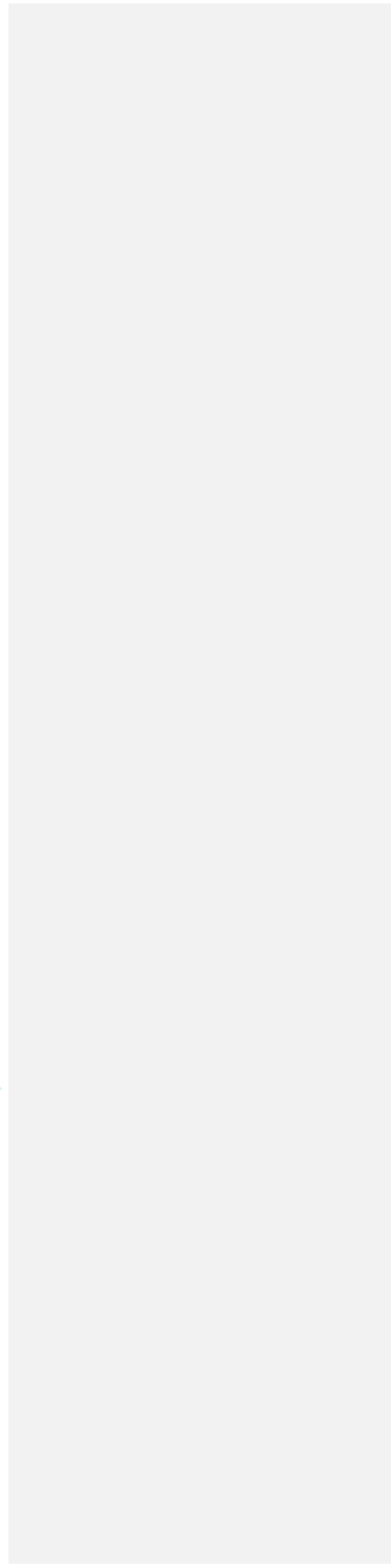
464 PIF3 like (PILs) are also basic helix loop helix transcription factors with large overlaps in
465 function to PIFs, but have been associated with shade avoidance (Li *et al.*, 2014). This overlap in
466 function has led to some ambiguous nomenclature as PIL5 is also referred to as PIF1 and likewise
467 PIL6 as PIF5 (Li *et al.*, 2014). PIL1 has a distinct function and was shown to work with TOC1 to restrict
468 growth at specific times of day (Salter *et al.*, 2003). PIL1 accumulates rapidly within the first hour of
469 shade cover acting as part of a rapid signalling pathway to stop growth (Li *et al.*, 2014), a secondary
470 longer lasting shade response is then mediated by HFR and phytochrome rapidly regulated (PAR1/2)
471 (Galstyan *et al.*, 2011). The exact mechanism through which PIL1 halts growth in shade is not known
472 but a number of hypothesis were presented in (Li *et al.*, 2014). It was suggested that as PIF1 has a
473 binding site for phyB it is possible that in shade PIL1 may outcompete PIF for DNA binding sites on
474 the Pfr form of phyB, therefore reducing the growth promoting function of PIF5 (Li *et al.*, 2014).
475 Alternatively, PIL1 may work via a PIF independent mechanism on components of downstream
476 pathways; however this is yet to be tested.

477
478 **HFR**

479 Long hypocotyl in far red 1 (HFR1) is a basic helix loop helix transcription factor involved in
480 phytochrome-mediated signalling (Fairchild *et al.*, 2000), and photomorphogenesis (Yang *et al.*,
481 2005). HFR is unstable in darkness and accumulates in the light, this accumulation is due to light
482 preventing COP1 mediated degradation of HFR (Yang *et al.*, 2005). HFR is not able to bind phyA or B
483 directly, instead HFR binds PIF3 forming potentially a heterodimer of PIF3/HFR which can then bind
484 to the Pfr form of phyA/B. This is also highlighted by the fact that HFR is more abundantly found in
485 far red light (Fairchild *et al.*, 2000). Mutants deficient in HFR had defective phyA responses, such as
486 hypocotyl elongation, and induction of chlorophyll A binding protein (CAB) (Fankhauser & Chory,
487 2000). HFR is also thought to have a blue-light response (Duek & Fankhauser, 2003) through CRY1
488 (Yang *et al.*, 2005), but the exact mechanism through which this occurs is not known.

489

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490 Intersection of the clock components ELF3- and ELF4 to light and clock signalling: major integrators
491 of light to the clock

492 *EARLY FLOWERING 3 (ELF3)* was first identified as a negative regulator of flowering time. In
493 addition to the observation that *elf3* mutant was shown to be early flowering, large circadian defects
494 were identified (Hicks *et al.*, 1996, Roden *et al.*, 2002; Undurraga *et al.*, 2012). *elf3* mutants are
495 defective in gating of red-light perception to the clock. Cloning of ELF3 allowed for interactors to be
496 detected, phyB was revealed to be a factor that associated to the N-terminus of ELF3 (Liu *et al.*,
497 2001). ELF3 was identified as playing a role in light signalling, in 12hours light 12 hours dark
498 entrainment, ELF3 accumulates in the nucleus just before darkness (ZT12) (Liu *et al.*, 2001).
499 Increasing day length, increases the nuclear accumulation of ELF3, increased darkness causes
500 accumulation of ELF3 to decrease to an undetectable level (Liu *et al.*, 2001) showing a direct
501 relationship between light and ELF3.

502 Phase response curves are made by measuring circadian period and phase during light
503 pulses, at times across subjective day and night. Phase response curves for wild-type Arabidopsis
504 in both red and blue light show the greatest effect and subsequent clock resetting to be caused by a
505 light pulse during the subjective night. *ELF3* overexpression lines showed a much more gradual
506 change in phase response with the same light pulses (Covington *et al.*, 2001). In white light, *ELF3*
507 overexpression causes a period lengthening effect in a light-dependent manner. In darkness, the
508 oscillator pace is not altered (Covington *et al.*, 2001). In *elf3* mutants, phase response light pulses
509 showed a much greater effect than the wild type, suggesting that clock resetting is light dependent
510 (Covington *et al.*, 2001), involving ELF3 in oscillator resetting by repressing the light input to the
511 clock (Bujdoso & Davis, 2013). However, the exact mechanism through which this occurs is
512 unknown.

513 *elf3* and *phyB* mutants were found to have similar phenotypic traits, such as hypocotyl
514 elongation in red light and constitutive shade avoidance (Devlin *et al.*, 1999). *elf3* mutants are also
515 defective in their response to blue and/ or red light with stronger effects showing in red light. ELF3
516 grown in darkness is rhythmic with a long-period phenotype, rhythmic in light/dark entrainment
517 cycles, but arrhythmic in free run light conditions (Hicks *et al.*, 1996). *elf3* plants are also unable to
518 inhibit hypocotyl elongation under light (Zagotta *et al.*, 1996). The combined phenotypic
519 characteristics of the *elf3* mutants suggest that ELF3 plays a role in light perception and signalling,
520 particularly in red light due to the interaction between ELF3 and phyB (Reed *et al.*, 2000).

521 *EARLY FLOWERING 4 (ELF4)* was the first clock component interpreted as being required for
522 the clock to cycle and it was revealed to be a component of normal light perception. Genetic loss of
523 *ELF4* resulted in plants that were markedly attenuated in the ability of a red-light pulse to generate
524 *CCA1* and *LHY* rhythms in etiolated plants. This was concluded to be due to ELF4 being required for
525 the phytochrome-mediated light induction of *CCA1* and *LHY* expression (Kikis *et al.*, 2005).
526 Consistent with this, it was shown that *elf4* mutants were hypermorphic and hypomorphic to red-
527 light cues, dependent on the assay. Notably, red-light mediated induction of *CAB2* expression was
528 elevated in *elf4* (McWatters *et al.*, 2007). This revealed that ELF4 contributes to so-called circadian
529 gating of light responsiveness (negative photomorphogenesis), light-regulation of *PIF4/5* expression
530 and the suppression of growth (positive photomorphogenesis) (Nozue *et al.*, 2007).

531 The presence of ELF4 in the nucleus increases the accumulation of ELF3 (Herrero *et al.*,
532 2012). ELF4 may function as a nuclear anchor for ELF3, but does not affect the nuclear localisation of
533 LUX, the third component of the evening complex (Herrero *et al.*, 2012). Nuclear import of phyB is
534 light dependent (Kircher *et al.*, 1999, Sakamoto & Nagatani, 1996), and it was shown that phyB does
535 not import ELF3 into the nucleus (Bujdoso & Davis, 2013). It is possible that ELF3 plays a role in the
536 nuclear import of phyB, as the N-terminus of ELF3 interacts with the C-terminal end of both the Pr
537 and Pfr forms of PHYB (Liu *et al.*, 2001). However, ELF3 and phyB have opposite roles in controlling
538 circadian oscillations (Herrero *et al.*, 2012). ELF3 needs the association with ELF4 to maintain
539 circadian oscillations, counteracting the COP1 and phyB mediated repression of ELF3 (Herrero *et al.*,
540 2012). ELF3 is also part of the blue-light signalling pathway, through its interaction with COP1. How

541 phyB and ELF4 coordinate the action and localisation of ELF3 seems critical for the cooperative
542 intersection of light perception and circadian clock function.

543 It was originally unclear what overall effect ELF3 has on other clock genes as the *elf3* loss of
544 function mutation causes arrhythmicity. A reduction-of-function mutation in *elf3-12* provided a way
545 to explore this, as the hypomorphic *elf3-12* allele is able to maintain rhythmicity (Kolmos *et al.*,
546 2011). This showed *elf3-12* to be light dependent but with a defective phase resetting mechanism.
547 This *elf3-12* mutant allowed the position of ELF3 within the clock to be derived as key to the
548 regulation of *PRR9* expression (Kolmos & Davis, 2007, Kolmos *et al.*, 2011). It is known that ELF3
549 associates to the promoter of *PRR9* to mediate its repression. In addition to clock-regulated *PRR9*
550 transcription, *PRR9* expression is also light regulated. Furthermore, *prp9* mutants display
551 photomorphogenic phenotypes (Nakamichi *et al.*, 2005). This highlights the role of ELF3 in
552 reciprocally linking light signalling to clock function.

553 Overexpression of *PHYA* in an *elf3-12* background showed that the overexpressed *PHYA* has
554 an additive effect with the *elf3-12* mutation to give a further shortened period in red light. In a range
555 of light conditions the *elf3-12 PHYA*-overexpression lines had an altered phase however in darkness
556 there was no change suggesting that light has an epistatic effect on *PHYA* (Kolmos *et al.*, 2011).
557 Overexpression of *PHYB* in the same *elf3-12* background gave the same period shortening as the
558 *PHYA*-overexpression lines; however the *PHYB-elf3-12* lines had a phase more closely linked to *PHYB*
559 overexpression in a wild-type background (Kolmos *et al.*, 2011). This result suggests that *PHYB*
560 functions upstream of *elf3-12* in light signalling and is able to suppress the effects of *elf3-12* (Bujdoso
561 & Davis, 2013). Together it appears that some, but not all, inputs of phytochromes to the clock
562 depend on ELF3.

563
564 Duration and quality of light

565 In regular light-dark cycles Arabidopsis has a circadian period of approximately 24 hours in
566 light, whereas in darkness it has a period of 30 to 36 hours (Millar *et al.*, 1995). Light therefore
567 makes the clock run faster, the absence of light cues causes the clock to slow, this is in keeping with
568 Aschoff's rule (Aschoff, 1979). The range of photoreceptors present in Arabidopsis allow a range of
569 fluence rates to be detected, ensuring the phase of the circadian oscillator is synchronised with
570 environmental cues (Somers *et al.*, 1998a), at both dawn and dusk (Devlin & Kay, 2000a). Removal or
571 even partial reduction of blue and red photoreceptors causes the clock to run slower (Millar *et al.*,
572 1995), suggesting that the effects of light intensity on the speed of the clock is limited by the number
573 of photoreceptors present. This would also suggest that it would not be possible to increase the
574 speed of the clock with higher light intensities beyond the maximum speed obtainable by that
575 number of photoreceptors.

576 Input of duration and quality of light are important in synchronising processes such as
577 flowering time and development (Weston *et al.*, 2000). Preceding photoperiod was shown to alter
578 the subsequent speed of the clock (Darrah *et al.*, 2006; Boikoglou *et al.* 2011). Interestingly here is
579 the long known role of ELF3 in processing light information to the clock (Hicks *et al.* 1996), and how
580 this coordinates the capacity for a plant to perceive daily boundaries present in a day night cycle
581 (McWatters *et al.* 2000). Recent work has revealed that extensive allelic variation at *ELF3* contribute
582 to alterations in photoperiodic control and this is associated to alterations in encoded nuclear
583 abundance and *in vivo* turn over diurnal time (Undurraga *et al.* 2012, Anwer *et al.* 2014). Combined
584 with temperature variation over the day, light duration gives information on the time of year or
585 season and therefore a warning of the growth conditions to follow. It is clear that allelic variation
586 exists in Arabidopsis to change the output of such varying entrainment processes (Darrah *et al.*,
587 2006, Boikoglou *et al.* 2011; Anwer *et al.* 2014).

588 Plants are able to adapt to changes in light intensity, such as consistently low light intensity,
589 by re-arranging photosynthetic machinery to be more efficient at light harvesting (Weston *et al.*,
590 2000). Blue light plays a major role in this. As such it would be assumed that cryptochromes and
591 *PHYA/B* play a role in directing the timing of light capture. A connection hub for this, *COP1* has been

592 identified as a signalling intermediate between these two processes (Walters *et al.*, 1999), however
593 links between photoreceptor function and organisation of the photosynthetic apparatus await
594 further investigation (Walters *et al.*, 1999, Weston *et al.*, 2000). Finally light intensity is also detected
595 by the plastid sensing blue light, causing structural changes and elongation of the palisade to absorb
596 more light, this process responds a lot more to blue light than red (Weston *et al.*, 2000). It could be
597 hypothesised that this plastid information is used as a nuclear clock and is synchronised with the
598 phyA and phyB red light input to the central oscillator by COP1.
599

600 Discussion

601 Multiple photoreceptors are essential components of light input to the clock. In this way
602 they play a central role in the light input to the clock. Not only with the reversible, light-mediated
603 reactions for maximal efficiency in light or dimmer light / shade, they also directly input light into the
604 central oscillator through clock associated factors, such as ELF3/4, COP1, ZTL, PIFs, PILs and HFR.
605 Transcriptional regulation and post-translational processes are all part of this complex web of
606 interconnections between light-perception and clock function. Overall light input to the clock forms
607 complex feedback systems that generated harmonised regulatory pathways, the mechanisms from
608 light perception to clock function, and back again, awaits clear discoveries.

609 Many plant growth chambers are produced with red, blue and far-red LED panels, but are
610 these the optimal light regimes to measure plant gene expression under? Furthermore, most
611 chambers have a lights-on or off function which does not represent the graded changes in intensity
612 that would occur with a plant growing under natural sunlight (or in a greenhouse), with the gradual
613 appearance and disappearance of light at sunrise and sunset. As white light comprises a combination
614 of different wavelengths of light simultaneously, it may be possible that the pathways for different
615 colours of light interact more than has been found so far. Overlapping functions have been found
616 between blue and red light and these are the most commonly used light wavelengths for plant LEDs.
617 It is possible that there are essential -components missing in just red and blue, although difficult to
618 isolate in a complex web of circadian gene expression, may only be present in white light or in other
619 light combinations not yet tested.

620 Light is essential for plant growth and it is therefore important to understand how plants
621 process the daily light cues they receive. Further understanding of how each light wavelength is
622 detected and the information fed into the central oscillator from each sensor, could potentially have
623 a large impact on plant and ultimately crop growth. With global changes in climate, knowledge on
624 essential lighting requirements and how this impacts on overall plant health could be used to
625 optimise crop productivity. Indoor farming techniques using LEDs as a light source could be
626 optimised for maximal yield and growth speed. As permafrost regions recede, and suitable growth
627 land becomes available. A detailed understanding of photoperiodicity and how it impacts fitness will
628 help with the challenges created by growing crops in shorter growth seasons and longer daylight
629 hours.

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632 Figure legends

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634 **Figure 1.** Schematic diagram of feedback loops in the Arabidopsis central oscillator.

635

636 **Figure 2.** Effects of light intensity on circadian period. A). Circadian gene expression is rhythmic in
637 constant light but in the absence of exogenous sucrose, rapidly becomes arrhythmic in prolonged
638 darkness. B). Following Aschoff's rule, high intensity light causes the clock to run faster; lower light
639 intensities cause the clock to slow. C). High light intensities result in period shortening; lower light
640 intensities result in period lengthening.

641

642 **Figure 3.** Circadian photoreceptors and their potential interactions to input light to the central
643 oscillator.

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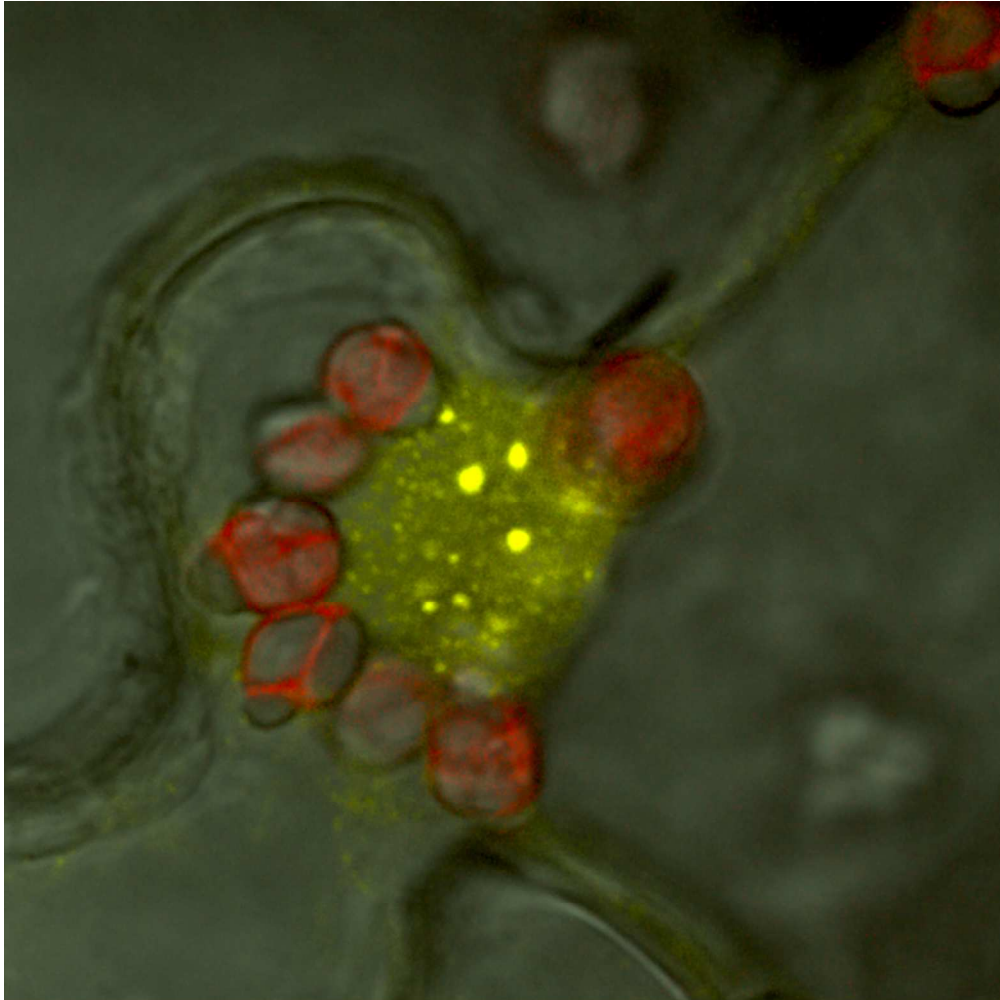
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ELF3 localisation: a master integrator of light-input to the circadian clock

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