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# AN EXTENSION OF THE KREMERS/VAN NORREN MODEL FOR RE_NAL LIGHT DAMAGE AND CONSEQUENCES THEREOF FOR OCCUPATIONAL SAFETY

13





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SUMMARY

The Kremers/Van Norren model gives a comprehensive across species description of retinal light damage threshold as a function of exposure time. It is based upon the assumptions a) that absorption in pigments in retina and pigment epithelium produces a toxic agent; b) that at sub-bleaching light levels the main mediating pigment is rhodopsin; and c) that at supra-bleaching level other pigments, possibly rhodopsin bleach products, take over.
In the first part of this report we have verified the validity of a few silent assumptions in the Kremers/Van Norren model: the neglection of the dynamic nature of the bleach process; the assumption that it is the maximum concentration of the toxic agent that determines the degree of damage; and the assumption that there is no cumulative effect of residual damage. The first assumption proved to be entirely justified. The second one not, but the mathematics of the original Kremers/Van Norren description remain valid when we apply their $3.5 * 10^5$ time constant to the repair process, rather than to the toxic agent resorption. As to the last assumption, the consequences of a cumulative residual damage mechanism are quantified.
In the second part we have tried to draw consequences for practice. This is done in two ways. In the first place the results of the model computations were converted to convential Threshold Limit Values (TLVs) to make them comparable to current safety standards. It is shown that, on the basis of the model interpretation, these need considerable revision in the long term exposure domain. In the second place the significance is discussed for sunglass prescription. It is shown that requirements for visual comfort run greatly parallel to requirements for ocular safety.

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**Een uitbreiding van het Kremers/Van Norren model voor lichtschade aan het netvlies, en de consequenties voor de veiligheid van het oog**

J.J. Vos

SAMENVATTING

Het Kremers/Van Norren model geeft een volledige beschrijving van het verloop van de schadedrempel met de expositieduur. Het is gebaseerd op drie aannamen: a) de oorzaak is de aanmaak van een giftige stof bij de absorptie van licht in pigmenten in netvlies en pigment-epiteel; b) zolang rhodopsine nog niet is weggebleekt, is dat de hoofdproducent; en c) wanneer dat is weggebleekt, nemen andere pigmenten (maar mogelijk de bleekproducten van rhodopsine) deze functie over.
In het eerste deel van dit rapport hebben we een aantal stilzwijgend gemaakte vereenvoudigingen in het Kremers/Van Norren model op hun geldigheid getoetst: dat het dynamisch karakter van het bleekproces mocht worden veronachtzaamd; dat de lichtschade zou worden bepaald door de maximale concentratie van de toxische stof; en dat er geen cumulatieve effecten optreden doordat lichtschade nooit helemaal wegtrekt.
De eerste aanname bleek geheel gerechtvaardigd. De tweede aanname niet, maar de gehele berekening volgens het Kremers/Van Norren model blijft geldig wanneer we de tijdconstante van $3.5 * 10^5$ s op het weefselherstel betrekken i.p.v. op de resorptie van de toxische stoffen. Wat betreft de derde aanname: we hebben de consequenties onderzocht van een cumulatief residu-effect.
In het tweede deel worden de consequenties bezien van het rekenmodel voor de practijk. Allereerst werden de resultaten omgerekend tot conventionele veiligheidsrichtlijnen, waardoor ze vergelijkbaar werden met gangbare voorschriften. Daaruit bleek dat deze, op basis van het model, aanmerkelijk zouden moeten worden aangepast in het domein van de langdurige blootstellingen. In de tweede plaats werden de gevolgen bezien voor het verstrekken van zonnebrillen. De wenselijkheid daarvan op grond van comfort bleek aardig samen te gaan met de wenselijkheid op grond van oogbescherming tegen lichtschade.

# 1 INTRODUCTION

Since the early sixties we know that light, even at subthermal irradiation levels, can damage the retina. The possibility of this 'abiotic' nature of light damage was already mentioned by Deutschmann (1882), but after the virtually exhaustive study by Verhoeff and Bell (1916) the thermal nature of retinal light damage was generally accepted. Verhoeff and Bell's explanation was questioned, though, when Vos (1962), by actually calculating the retinal temperature rise in the sun's image, proved that this was too low to explain the damage. In 1966 Noell et al. published their famous discovery of low light level damage in the rat retina, which they attributed to phototoxic effects. The action spectrum turned out to be similar to that of rhodopsin, which pointed to a photoreceptor site for the damage mechanism. In the late seventies Ham et al. (1976) identified, in experiments on monkeys, another photic damage mechanism with a completely different action spectrum peaking around the short wavelength limit of the visual spectrum and therefore often called 'blue light hazard'. Instead of the long term, low level characteristics of the Noell type phototoxic damage, the Ham type typically occurred during short term, high level exposures. For a recent review we refer to Ham and Müller (1989).

The two damage mechanisms lived separate scientific lives until Kremers and Van Norren (1988), while bringing together all then available literature data on white light exposure thresholds into one time versus irradiance plot (Fig. 1), discovered that they nicely lined up - with notable gaps, to be true - along a theoretically understandable time course. The turn over from Noell to Ham type nicely corresponded with the $10^4$ to $10^5$ troland range in which virtually all bleaching occurs. With all visual pigment bleached the Noell type damage inducing agent is gone and the less effective Ham type agent, possibly the rhodopsin bleach product(s), take over.
Until recently, this unifying model was only a hypothesis; but new experimental evidence has brought corroboration. Not only have the gaps been reduced (Kremers and Van Norren, 1989), but, more importantly, Rapp et al. (1989) and Van Norren and Schellekens (1990) have shown that rats can suffer Ham type photic damage as well. That both Ham and Noell type of damage have now been shown in one animal model makes Kremers and Van Norren's across animal generalization less hypothetical. With regard to the susceptibility of the human retina the main uncertainty, then, is in damage thresholds for low irradiation levels. Although Noell type of damage has been observed in

monkey (Sykes et al., 1981), no primate data are available below 4 $W/m^2$.

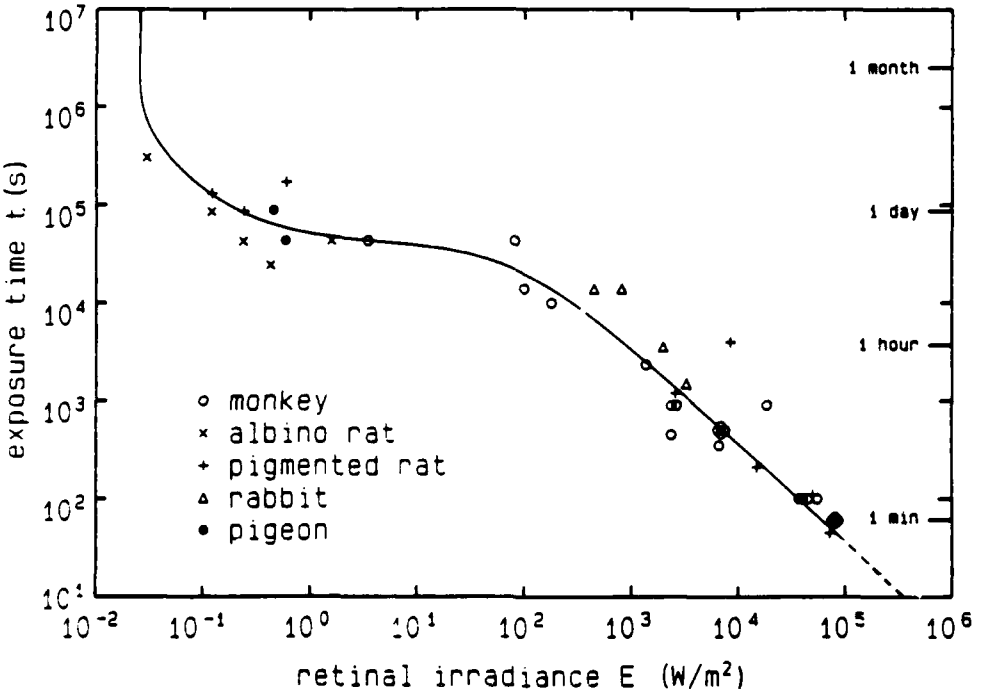


Fig. 1 Photic threshold damage data for rat, monkey, rabbit and pigeon for white light exposure. Data are from various sources, as tabulated by Kremers and Van Norren (1989; only threshold and interpolated threshold data from their Table 1), supplemented with data from Van Norren and Schellekens (1990). The drawn curve is the best fitting semitheoretical across animal relation (Eq. 11 in this report). The right-hand end is drawn as a dashed line as one that enters the retinal burn domain.

Yet we consider the curve shown in Fig. 1 as the best available approximation of the light damage threshold versus exposure time course for probably all mammals. It consists of two branches: left the Noell branch with photoreceptor pigment characteristiscs, and right the Ham branch with a UV peaking action spectrum.

In this report we will first refine and extend the Kremers/Van Norren model in a number of respects (Ch.2). After that we will discuss the possible consequences of this model interpretation for ocular safety (Ch.3). Herein we will pay attention to Threshold Limit Values in the long term exposure domain and to the significance of these values for eye protection by sunglasses.

# 2 GENERALIZATION OF THE KREMERS/VAN NORREN MODEL

In this chapter we will first repeat, in a slightly revised (section 2.1) and extended (section 2.2) version, the original derivation by Kremers and Van Norren. This derivation is based upon a few silent assumptions, and the validity of these assumptions is tested in the subsequent sections 2.3 and 2.4. Finally we will discuss the consequences of the model for chronic exposure in section 2.5.

## 2.1 Description by one formula of the original model

Kremers and Van Norren (1988) gave a mathematical description which needs some generalization to make it applicable for other light sources than broad band white. The basic assumption is that two pigments, rhodopsin (R), and its bleach product(s) (B)[1)] are intermediate to produce the toxic agent, with concentration C. This concentration is governed by the first order differential equation

$$\frac{dC}{dt} = (\eta E)_R + (\eta E)_B - \frac{C}{\tau} \qquad (1)$$

in which $(\eta E)_{R,B}$ represent the production rates by rhodopsin and by the bleach products:

$$(\eta E)_R = \eta_R \, P \int E_\lambda N_\lambda d\lambda = \eta_R \, P.E \int \varepsilon_\lambda N_\lambda d\lambda = \eta_R \eta_N \, P.E \qquad (2)$$

and

$$(\eta E)_B = \eta_B \, (1\text{-}P) \int E_\lambda H_\lambda d\lambda = \eta_B \, (1\text{-}P).E \int \varepsilon_\lambda H_\lambda d\lambda = \eta_B \eta_H \, (1\text{-}P).E \qquad (3)$$

Herein $N_\lambda$ and $H_\lambda$ represent the Noell and the Ham type of light damage spectra holding for the R- and the B-mediated damage, respectively. Convoluted with the normalized retinal stimulus spectrum ($\varepsilon_\lambda$) they determine the radiation efficacies $\eta_N$ and $\eta_H$. These are to be distinguished from the intrinsic toxic efficacies $\eta_R$ and $\eta_B$ of the two pigments involved. The constant $\tau$ is the time constant of the toxic agent resorption process. Finally, P represents the fraction rhodopsin unbleached. According to Rushton (1972)

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[1)] An alternative presumption might be that not the bleaching product(s) but other pigment(s) are intermediate (cf. Sliney, 1988). This does not lead to a markedly different description, though.

$$P = \frac{E_0}{E + E_0} \qquad (4)$$

for a particular light source. For their UV- and IR-filtered Xenon light source ($Xe_f$) Kremers and Van Norren (1988) calculated $E_0 = 0.2$ $W/m^2$. For other light sources we have to generalize (4) by taking into account that E is weighted by the rhodopsin action spectrum, i.e. $N_\lambda$. Then

$$P = \frac{E_0 \int \varepsilon_\lambda N_\lambda d\lambda}{E \int \varepsilon_\lambda N_\lambda d\lambda + E_0 \int \varepsilon_\lambda N_\lambda d\lambda} = \frac{\eta_N E_0}{\eta_N E + \eta_N E_0}$$

in which $\eta_N E_0$, the effective half-bleach excitation level, is always the same and thus equals the value for the $Xe_f$ light source, for which we have calculated (see Table II) $\eta_N = 4.2 * 10^{-3}$. Consequently

$$\eta_N E_0 = 4.2 * 10^{-3} * 0.2 = 8.4 * 10^{-4} \text{ W/m}^2, \text{ and}$$

$$P = \frac{8.4 * 10^{-4}}{\eta_N E + 8.4 * 10^{-4}} = \frac{1}{1 + 1200\ \eta_N E} \text{ and thus } 1\text{-}P = \frac{1200\ \eta_N E}{1 + 1200\ \eta_N E} \qquad (5)$$

By substituting (2), (3) and (5) into (1) we obtain

$$\frac{dC}{dt} = \eta_R \eta_N \frac{E}{1 + 1200\ \eta_N E} + \eta_B \eta_H \frac{1200\ \eta_N E^2}{1 + 1200\ \eta_N E} - \frac{C}{\tau}, \text{ or}$$

$$\frac{dC}{dt} = \frac{\eta_B \eta_H E}{1 + 1200\ \eta_N E} \left( 1200\ \eta_N E + \frac{\eta_R \eta_N}{\eta_B \eta_H} \right) - \frac{C}{\tau} \qquad (6)$$

This differential equation does only differ from Kremers and Van Norren's formulation in that it combines the two damage mechanisms in one equation and thus produces one predicted damage threshold relation over the whole exposure domain.

The solution of this differential equation is

$$C = \frac{\eta_B \eta_H E \tau}{1 + 1200\ \eta_N E} \left( 1200\ \eta_N E + \frac{\eta_R \eta_N}{\eta_B \eta_H} \right) (1 - e^{-t/\tau})$$

or

$$t = -\tau \ln \left[ 1 - \frac{C}{\tau} \frac{1 + 1200\ \eta_N\ E}{\eta_B \eta_H\ E\ (\ 1200\ \eta_N\ E + \frac{\eta_R \eta_N}{\eta_B \eta_H}\ )} \right]$$

For a fixed critical value $C_{thr}$ this equation describes the threshold relation between exposure time t and retinal irradiance E:

$$t = -\tau \ln \left[ 1 - \frac{C_{thr}}{\tau} \frac{1 + 1200\ \eta_N\ E}{\eta_B \eta_H\ E\ (\ 1200\ \eta_N\ E + \frac{\eta_R \eta_N}{\eta_B \eta_H}\ )} \right] \qquad (7)$$

Assuming that, with ordinary light sources $\eta_R \eta_N \gg \eta_B \eta_H$ (see later), we can distinguish three main branches:

$1200\ \eta_N\ E \ll 1$: $\qquad t = -\tau \ln \left[ 1 - \frac{C_{thr}}{\tau\ \eta_R \eta_N\ E} \right]$

which means that there is a vertical asymptote

$$E_{as} = \frac{C_{thr}}{\tau\ \eta_R \eta_N} \qquad (8)$$

$1 \ll 1200\ \eta_N\ E \ll \frac{\eta_R \eta_N}{\eta_B \eta_H}$ : $\quad t = -\tau \ln \left[ 1 - \frac{C_{thr}}{\tau} \cdot \frac{1200\ \eta_N\ E}{\eta_R \eta_N\ E} \right]$

which means that there is a plateau at

$$t_{hor} = \frac{C_{thr} * 1200}{\eta_R} \qquad (9)$$

$1200\ \eta_N\ E \gg \frac{\eta_R \eta_N}{\eta_B \eta_H}$ : $\quad t = -\tau \ln \left[ 1 - \frac{C_{thr}}{\tau} \cdot \frac{1}{\eta_B \eta_H\ E} \right] \approx \frac{C_{thr}}{\eta_B \eta_H\ E}$

which means that the threshold relation bends down under 45° with

$$(E * t)_{diag} = \frac{C_{thr}}{\eta_B \eta_H} \qquad (10)$$

For the filtered Xenon light source we calculated (see Table II) $\eta_H = 3.2*10^{-4}$ and $\eta_N = 4.2*10^{-3}$. Furthermore we can read from Fig. 1:

$$t_{hor} = 4 * 10^4 \text{ s and } (E * t)_{diag} = 3.5 * 10^6 \text{ J/m}^2$$

Unfortunately the scarce data below 0.1 W/m$^2$ do not allow an accurate determination of $E_{as}$. We can better rely upon Griess and Blankenstein's (1981) independent determination of the recovery time constant $\tau = 3.5 * 10^5$ s [2)]. By substituting the above values and dividing (8) by (9) we obtain $E_{as} = 0.02$ W/m$^2$; by dividing (9) by (10) $\eta_R \eta_B = 35$; and by dividing (8) by (10) $\eta_R \eta_N / \eta_B \eta_H = 500$. This confirms our initial presumption that $\eta_R \eta_N >> \eta_B \eta_H$.
As a result eq. (7) reduces to

$$t = - 3.5 * 10^5 \ln \left[ 1 - \frac{1 + 1200\ \eta_N E}{300\ \eta_H E\ (1200\ \eta_N E + 35\ \eta_N/\eta_H)} \right] \qquad (11)$$

This formula gives the generalized description of the Kremers/Van Norren two pigment light damage model. On the basis of the $\eta_H, \eta_N$-values for the filtered Xenon source it produces the line drawn in Fig. 1 which, given the variety of methods of damage evaluation and animal models, satisfactorily fits the experimental threshold data. In the next section we will deal with the radiation efficacies of other light sources.

## 2.2 The radiation efficacies of various light sources

In order to determine the radiation efficacies $\eta_N$ and $\eta_H$ for an arbitrary light source, we have to convolute the action spectra with the ***normalized retinal*** light spectrum $\epsilon_\lambda$. Herein 'normalized' means

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[2)]Actually, Kremers and Van Norren (1988) speak of $\tau$ in terms of the toxic agent decay time, whereas Griess and Blankenstein (1981) speak in terms of the repair time. We will come back to this difference in section 2.4. In anticipation, we may use here this $\tau$-value, formally only determined in the Ham domain, for the whole Noell/Ham domain, as tissue repair does not depend on the primary cause of damage.

$$\int \varepsilon_\lambda d\lambda = 1$$

and 'retinal' that we have to take into account the light losses due to absorption in the eye media (transmission factor $T_\lambda$). Table I lists the values used for the calculations.

Table I Spectral data needed to calculate the radiation efficacies for various light sources.

| λ (nm) | $T_\lambda$ eye media | $\varepsilon_\lambda$ filtered Xenon * $10^{-3}$ | $\varepsilon_\lambda$ Xenon lamp * $10^{-3}$ | $\varepsilon_\lambda$ halogen * $10^{-3}$ | $\varepsilon_\lambda$ TL soft white * $10^{-3}$ | $\varepsilon_\lambda$ sunlit snow * $10^{-3}$ | $\varepsilon_\lambda$ sunlight * $10^{-3}$ | $N_\lambda$ action sp. * $10^{-3}$ | $H_\lambda$ action sp. * $10^{-3}$ |
|---|---|---|---|---|---|---|---|---|---|
| 345 | 0.0080 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0 | 15.5 |
| 355 | 0.0035 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.7 | 15.5 |
| 365 | 0.0023 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.5 | 15.0 |
| 375 | 0.0025 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.4 | 13.9 |
| 385 | 0.0060 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.3 | 10.8 |
| 395 | 0.023 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.1 | 1.3 | 8.1 |
| 405 | 0.079 | 0.1 | 0.4 | 0.1 | 0.4 | 0.6 | 0.2 | 1.5 | 6.0 |
| 415 | 0.21 | 0.5 | 1.0 | 0.3 | 0.2 | 1.7 | 0.6 | 1.8 | 4.5 |
| 425 | 0.41 | 0.9 | 2.1 | 0.9 | 0.6 | 3.3 | 1.4 | 2.3 | 3.4 |
| 435 | 0.59 | 3.3 | 3.0 | 1.4 | 7.2 | 4.5 | 2.2 | 2.7 | 2.4 |
| 445 | 0.69 | 2.3 | 3.3 | 1.7 | 1.4 | 5.3 | 2.9 | 3.7 | 1.5 |
| 455 | 0.74 | 3.1 | 3.7 | 1.9 | 1.6 | 5.6 | 3.4 | 5.6 | 0.9 |
| 465 | 0.80 | 4.2 | 4.0 | 2.3 | 1.7 | 5.7 | 3.9 | 6.7 | 0.7 |
| 475 | 0.83 | 4.7 | 4.1 | 2.6 | 2.0 | 5.6 | 4.2 | 7.2 | 0.5 |
| 485 | 0.87 | 4.9 | 4.4 | 2.8 | 2.1 | 5.6 | 4.6 | 7.7 | 0.4 |
| 495 | 0.91 | 5.6 | 4.6 | 3.2 | 2.3 | 5.5 | 4.8 | 8.0 | 0.3 |
| 505 | 0.94 | 4.8 | 4.7 | 3.4 | 2.5 | 5.3 | 5.0 | 8.1 | 0.2 |
| 515 | 0.97 | 5.0 | 4.8 | 3.8 | 2.9 | 5.1 | 5.1 | 7.8 | 0.2 |
| 525 | 0.99 | 5.2 | 4.9 | 4.2 | 3.4 | 4.9 | 5.1 | 7.3 | 0.1 |
| 535 | 1.00 | 5.5 | 5.0 | 4.4 | 3.7 | 4.7 | 5.2 | 6.6 | 0.1 |
| 545 | 1.00 | 5.6 | 5.0 | 4.9 | 9.2 | 4.4 | 5.2 | 5.7 | 0 |
| 555 | 1.00 | 5.7 | 5.0 | 5.5 | 4.7 | 4.2 | 5.2 | 4.2 | 0 |
| 565 | 1.00 | 5.7 | 5.0 | 5.8 | 5.3 | 4.0 | 5.2 | 2.9 | 0 |
| 575 | 1.00 | 5.6 | 5.0 | 6.1 | 7.2 | 3.9 | 5.1 | 1.6 | 0 |
| 585 | 1.00 | 5.4 | 5.0 | 6.7 | 6.6 | 3.7 | 5.1 | 0.9 | 0 |
| 595 | 1.00 | 5.2 | 5.0 | 7.1 | 7.5 | 3.6 | 5.1 | 0.5 | 0 |
| 605 | 1.00 | 4.8 | 5.0 | 7.4 | 7.6 | 3.4 | 5.1 | 0.3 | 0 |
| 615 | 1.00 | 4.4 | 5.0 | 7.5 | 7.4 | 3.2 | 5.1 | 0.2 | 0 |
| 625 | 1.00 | 4.2 | 5.0 | 7.8 | 6.7 | 3.1 | 5.1 | 0.1 | 0 |
| 635 | 0.99 | 3.9 | 5.0 | 8.2 | 5.8 | 2.9 | 5.1 | 0 | 0 |
| | $\Sigma\varepsilon_\lambda$*10 nm | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |

All values of $\varepsilon_\lambda$, $N_\lambda$ and $H_\lambda$ are at human retinal level. Sources: $H_\lambda$ and filtered Xenon: Kremers and Van Norren (1989); other light sources: Wyszecki and Stiles (1967). For $T_\lambda$ we used the compiled literature data from Vos (1974), for $N_\lambda$ the scotopic luminosity function, divided by $T_\lambda$.

These spectral courses are also plotted in Fig. 2.

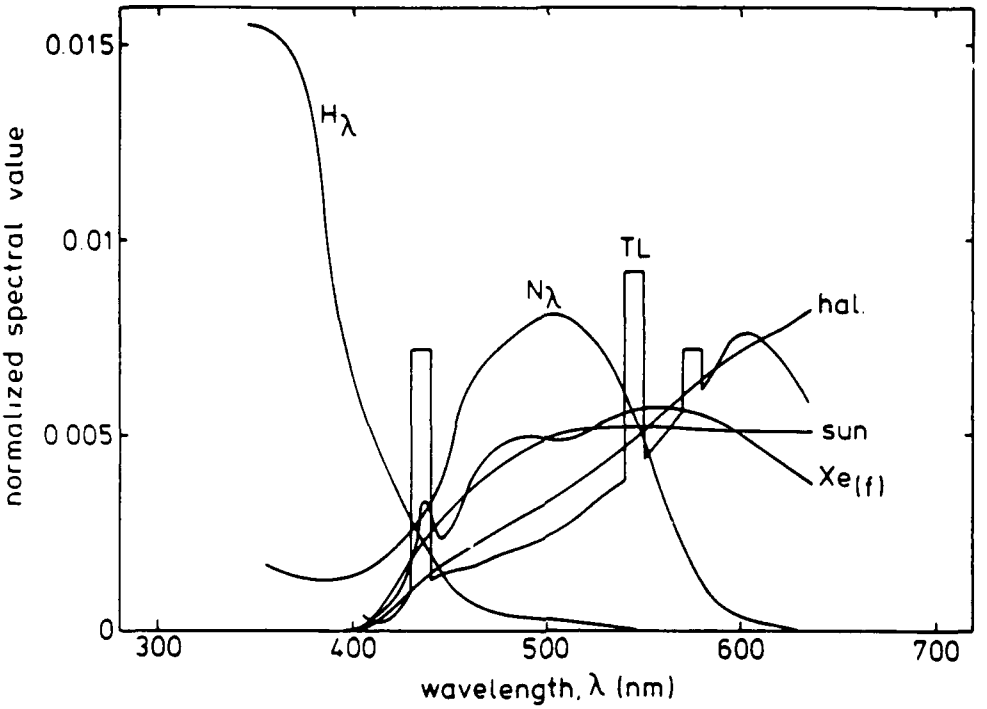


Fig. 2 Normalized emission spectra ($\varepsilon_\lambda$) for various light sources, taking into account intraocular transmission losses. Moreover, the retinal action spectra for the Noell ($N_\lambda$) and Ham ($H_\lambda$) damage mechanisms are shown, also at the retinal level.

The convolution integrals $\eta_N = \int \varepsilon_\lambda N_\lambda d\lambda$ and $\eta_H = \int \varepsilon_\lambda H_\lambda d\lambda$ are given in Table II.

Table II Calculated radiation efficacies for various white light sources.

| radiation efficacies | light sources | | | | | |
|---|---|---|---|---|---|---|
| | $Xe_f$ | Xe | Hal | TL soft white | snow | sun |
| $\eta_N$ | $4.2*10^{-3}$ | $4.0*10^{-3}$ | $3.1*10^{-3}$ | $3.0*10^{-3}$ | $4.6*10^{-3}$ | $4.1*10^{-3}$ |
| $\eta_H$ | $3.2*10^{-4}$ | $4.0*10^{-4}$ | $2.0*10^{-4}$ | $3.2*10^{-4}$ | $6.2*10^{-4}$ | $3.3*10^{-4}$ |
| $\eta_N/\eta_H$ | 13.1 | 10 | 15.5 | 9.4 | 7.4 | 12.3 |

The herewith calculated threshold damage relations [on the basis of eq. (7)] are plotted in Fig. 3 by drawn lines.

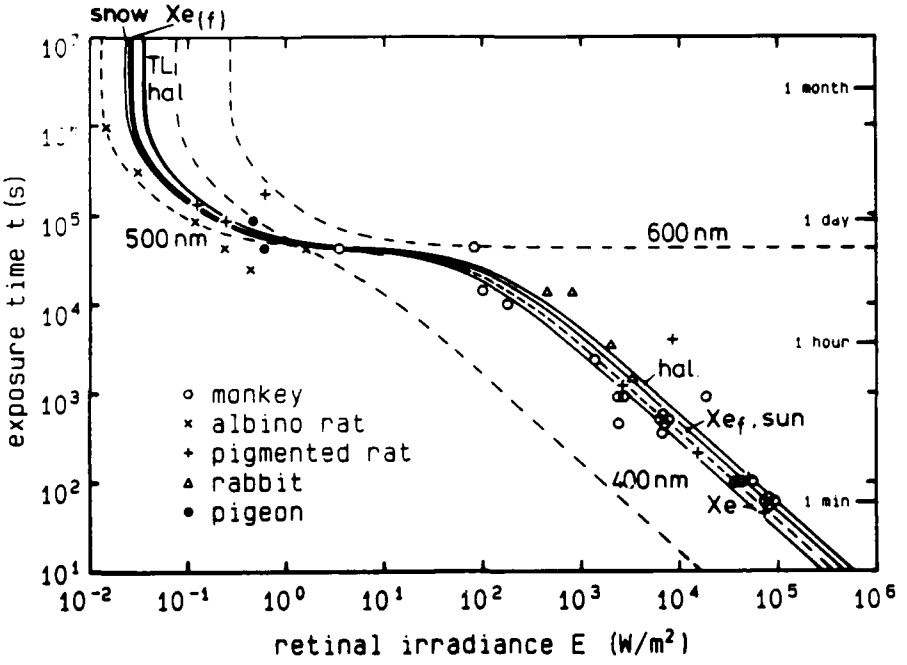


Fig. 3 Calculated threshold light damage relations for various light sources, both broad band white light (drawn) and monochromatic (interrupted). Xe = Xenon lamp; $Xe_f$ = UV- and IR-filtered Xenon; Hal = halogen; TL = soft white fluorescent light; snow = snow, illuminated by sun plus bright sky.

Apparently the various types of broad band white light do not differ greatly in their damaging provocation, and this may be a justification in retrospect of the way Kremers and Van Norren (1988) pooled all literature data into one graph. We left out the right hand part of the 'snow' and 'TL' curves as they never reach the irradiance levels in the Ham domain. Differences between curves become only marked, of course, when small band or monochromatic light is used as stimulus. Then $\eta_{N,H}$ reduce to $N_\lambda, H_\lambda$, so that

$$t = -3.5 * 10^5 \ln\left[1 - \frac{1 + 1200\, N_\lambda\, E}{300\, H_\lambda\, E\,(1200\, N_\lambda\, E + 35\, N_\lambda/H_\lambda)}\right] \quad (12)$$

For 400 nm the curve crosses the 'white' band due to the fact that the Noell damage mechanism ($N_\lambda$) is rather insensitive to far blue and the Ham mechanism ($H_\lambda$) typically more sensitive. At 600 nm the Ham mechanism is not activated at all and the Noell mechanism to a lesser degree than by white light. As can be checked by comparing $\eta_{N,H}$ for $Xe_f$

with the $N_\lambda, H_\lambda$-values listed in Table I, the $Xe_f$ course approximately coincides with that for 450 and 565 nm in the Noell domain, and with 500 nm in the Ham domain (same corresponding $\eta$-values). There is no single wavelength equivalent to white over the whole time/irradiance domain.

## 2.3 Inclusion of the dynamic characteristics of the bleach process

In section 2.1 P was taken as stationary at its final value, though we know that it changes during the irradiation. That means that the production of toxic agent via the Noell process during the first stage of high intensity irradiation is neglected. In this section we will look whether we were allowed to do so, a question which is not easily answered intuitively, since on the one hand the time to reach the static bleach level is short, but on the other hand, the Noell process has a higher toxic efficacy.

We return to the origin of eq. (4), i.e. the differential equation that governs P as a function of E:

$$\frac{dP}{dt} = - \eta_N E P + \frac{1-P}{T} \qquad (13)$$

in which T is the time constant of the rhodopsin regeneration process ($\simeq$ 600 s). The solution of (13) is

$$P = \frac{1}{1 + \eta_N E T} \left[ 1 + \eta_N E T \, e^{- \frac{1 + \eta_N E T}{T} t} \right] \qquad (14)$$

in which 1/T can be replaced by $\eta_N E_0$, with $E_0$ = half bleach irradiance of eq. (4):

$$P = \frac{\eta_N E_0}{\eta_N E + \eta_N E_0} + \frac{\eta_N E}{\eta_N E + \eta_N E_0} \cdot e^{- (\eta_N E_0 + \eta_N E) t} \qquad (15)$$

Herein $\eta_N E_0 = (\eta_N E_0)_{Xe_f} = 4.2 * 10^{-3} * 0.2 = 8.4 * 10^{-4}$ W/m$^2$, so that

$$P = \frac{1}{1 + 1200 \eta_N E} + \frac{1200 \eta_N E}{1 + 1200 \eta_N E} \cdot e^{- (8.4*10^{-4} + \eta_N E) t} \qquad (16)$$

This has to be substituted in

$$\frac{dC}{dt} = \eta_R\eta_N\ P\ E + \eta_B\eta_H\ (1-P)\ E - \frac{C}{\tau}\ :$$

$$\frac{dC}{dt} = \underbrace{\frac{\eta_R\eta_N+1200\eta_N E\eta_B\eta_H}{1+1200\eta_N E}}_{\varphi}\ E + \underbrace{\frac{(\eta_R\eta_N-\eta_B\eta_H).1200\eta_N E}{1+1200\eta_N E}}_{\psi}\ e^{-\overbrace{(8.4*10^{-4}+\eta_N E)}^{\alpha}t} - \frac{C}{\tau}$$

simplified to

$$\frac{dC}{dt} = \varphi + \psi\ e^{-\alpha t} - \frac{C}{\tau} \qquad (17)$$

The solution reads

$$C = p \cdot e^{-\alpha t} + q \cdot e^{-t/\tau} + r$$

the constants in which can be determined by substitution:

$$-\alpha p\ e^{-\alpha t} - \frac{q}{\tau}\ e^{-t/\tau} = \varphi + \psi\ e^{-\alpha t} - \frac{p}{\tau}\ e^{-\alpha t} - \frac{q}{\tau}\ e^{-t/\tau} - \frac{r}{\tau}\ ,\ \text{thus}$$

$p = \dfrac{\psi\tau}{1-\alpha\tau}$ and $r = \varphi\tau$. Further, at t=0, C=0, so that $q = -\varphi\tau - \dfrac{\psi\tau}{1-\alpha\tau}$

As a result

$$C = \frac{\psi\tau}{1-\alpha\tau}\ e^{-\alpha t} - \left(\varphi\tau + \frac{\psi\tau}{1-\alpha\tau}\right) e^{-t/\tau} + \varphi\tau \qquad (18a)$$

or, in full, with $\dfrac{\tau}{1-\alpha\tau} = \dfrac{1200\ \tau}{1200 - (1+1200\eta_N E)\ \tau}$

$$C = \frac{(\eta_R\eta_N-\eta_B\eta_H)\ 1200\ \eta_N\ E}{1\ +\ 1200\ \eta_N\ E} \cdot \frac{1200\ \tau}{1200 - (1+1200\eta_N E)\ \tau} \cdot e^{-\frac{1+1200\eta_N E}{1200}\,t}$$

$$-\left[\frac{\eta_R\eta_N+1200\eta_N E\eta_B\eta_H}{1+1200\eta_N E} \cdot E\ \tau + (\eta_R\eta_N-\eta_B\eta_H)\ \frac{1200\eta_N E}{1+1200\eta_N E} \cdot \frac{1200\ \tau}{1200-(1+1200\eta_N E)\tau}\right] *$$

$$* e^{-t/\tau} + \frac{\eta_R\eta_N\ +\ 1200\ \eta_N\ E\ \eta_B\eta_H}{1\ +\ 1200\ \eta_N\ E}\ E\ \tau \qquad (18b)$$

- With $t \ll \alpha^{-1} \ll \tau$ and $1200\ \eta_N\ E \gg \frac{\eta_R\eta_N}{\eta_B\eta_H} \gg 1$:

$$C = \varphi\tau\ (1-e^{-t/\tau}) = \varphi t = E * t * \eta_B\eta_H$$

$$\text{so that } \frac{C}{\eta_B\eta_H} = E * t = 3.5 * 10^6 \text{ at threshold for } Xe_f$$

- With $t \gg \tau$ and $1200\ \eta_N\ E \ll 1$: $\quad C = \psi\tau = \eta_R\eta_N\ E\ \tau$

Since $$E_{as} = \frac{C}{\eta_R\eta_N\ \tau} = 0.02\ W/m^2 \text{ we obtain}$$

$$\frac{C}{\eta_R\eta_N} = 0.02 * 3.5 * 10^5 = 7 * 10^3 \text{ and}$$

$$\frac{\eta_R\eta_N}{\eta_B\eta_H} = \frac{3.5 * 10^6}{7 * 10^3} = 500\ (\gg 1, \text{ indeed, for } Xe_f)$$

With $\left[\frac{\eta_N}{\eta_H}\right]_{Xe_f} = \frac{4.2 * 10^{-3}}{3.2 * 10^{-4}} = 13$ this yields $\frac{\eta_R}{\eta_B} = \frac{500}{13} = 38$

(a value which is not dependent on the light source). We can now refrase (18) for arbitrary light sources by taking

$$\frac{C}{\eta_B\eta_H} = \frac{C}{(\eta_B\eta_H)_{Xe_f}} \cdot \frac{\eta_{H_{Xe_f}}}{\eta_H} = \frac{3.5*10^6 * 3.2*10^{-4}}{\eta_H} = \frac{1120}{\eta_H}$$

Thus, eq. (18b) becomes

$$\frac{1120}{\eta_H} = -\left(38\frac{\eta_N}{\eta_H} - 1\right) \cdot \frac{1200\eta_N E}{1+1200\eta_N E} \cdot \frac{1200}{3.5*10^5+1200\eta_N E} \cdot e^{-\frac{1+1200\eta_N E}{1200}t}$$

$$-\left[\frac{38\eta_N/\eta_H+1200\eta_N E}{1+1200\eta_N E} \cdot 3.5*10^5 E - \left(38\frac{\eta_N}{\eta_H} - 1\right) \cdot \frac{1200\eta_N E}{1+1200\eta_N E} \cdot \frac{1200}{3.5*10^5+1200\eta_N E}\right] *$$

$$* e^{-2.86*10^{-6}t} + \frac{38\eta_N/\eta_H+1200\eta_N E}{1+1200\eta_N E} \cdot 3.5*10^5 E \qquad (19)$$

This equation is the dynamic equivalent of eq. (11). In how far does it differ? Not notably, since all the extra 'dynamic' terms completely vanish in comparison with their static counterparts:

$$\frac{\psi\tau}{1-\alpha\tau} \ll \varphi\tau \text{ and } e^{-\alpha t} \ll e^{-t/\tau}$$

which can be easily verified by substituting a few typical $\eta_N E$ values. By dropping these negligible parts of eq. (19) we indeed neatly return to eq. (11).

We conclude that the dynamic nature of the bleach process does not affect the Kremers/Van Norren model. We can and will stick, therefore, to the more simple description (11).

## 2.4 A two level description

The Kremers/Van Norren model restricts the discussion to what happens with the toxic agent. If C exceeds a criterion level, damage will result, independent of the time span over which the transgression occurs. Of course, this is too simple an assumption, and a better, second approximation description will be:

$$\text{light } E \xrightarrow{\tau} \text{toxic agent } C \xrightarrow{\theta} \text{tissue damage } D$$

The first part of this scheme was treated in section 2.1. We will now add the second part, to which we adhere a time constant $\theta$ for tissue repair. The mathematical equation is completely similar to that of the first equation:

$$\frac{dD}{dt} = k\,C - \frac{D}{\theta} \qquad (20)$$

Herein we will enter now the earlier (eq. 6) derived expression for C:

$$C = \alpha\tau\,(1 - e^{-t/\tau}) \quad (\text{for } t < t_{irr}) \qquad (21a)$$

here complemented with an after offset relation

$$C = \alpha\tau\,(1 - e^{-t_{irr}/\tau})\,e^{-(t-t_{irr})/\tau} \quad (\text{for } t \geq t_{irr}) \qquad (21b)$$

Herein $\alpha = \dfrac{\eta_B\eta_H E}{1+1200\eta_N E} \cdot \left( 1200\eta_N E + \dfrac{\eta_R\eta_N}{\eta_B\eta_H} \right)$ as earlier derived.

E = irradiance level in $W/m^2$ and $\tau$ = toxic agent resorption time in s.

We solve first eqs (20) and (21a):

$$\frac{dD}{dt} = k\alpha\tau\ (1-e^{-t/\tau}) - \frac{D}{\theta}$$

with the boundary condition that, at t = 0, D = 0. The solution reads

$$D = k\alpha\tau\theta \left[ 1 - \frac{\tau}{\tau-\theta} e^{-t/\tau} + \frac{\theta}{\tau-\theta} e^{-t/\theta} \right] \qquad (22)$$

Similarly we solve now eqs (20) and (21b):

$$\frac{dD}{dt} = k\alpha\tau\ (e^{t_{irr}/\tau} - 1)\ e^{-t/\tau} - \frac{D}{\theta} \qquad (23)$$

The general solution reads

$$D = \frac{\tau\theta}{\tau-\theta} k\alpha\tau\ (e^{t_{irr}/\tau} - 1)\ e^{-t/\tau} + \text{const} * e^{-t/\theta} \qquad (24)$$

The boundary condition, of course, is that eq. (23) = eq. (24) at $t_{irr}$; as a result we obtain

$$D = k\alpha\tau\theta \left[ \frac{\tau}{\tau-\theta} (e^{t_{irr}/\tau} - 1)\ e^{-t/\tau} - \frac{\theta}{\tau-\theta} (e^{t_{irr}/\theta} - 1)\ e^{-t/\theta} \right] \qquad (25)$$

Our interest now is: which is the maximum value D will attain. This maximum will certainly be reached after offset of the irradiation, so we will differentiate eq. (25):

$$\frac{dD/k\alpha\tau\theta}{dt} = - \frac{e^{t_{irr}/\tau} - 1}{\tau-\theta} e^{-t/\tau} + \frac{e^{t_{irr}/\theta} - 1}{\tau-\theta} e^{-t/\theta} = 0$$

which leads to

$$t_{max} = \frac{\tau\theta}{\theta-\tau} \ln \frac{e^{t_{irr}/\tau} - 1}{e^{t_{irr}/\theta} - 1} \qquad (26)$$

Substitution of (26) in (25) produces

$$\frac{D_{max}}{k\alpha\tau\theta} = (e^{t_{irr}/\theta} - 1)^{\theta/(\theta-\tau)} * (e^{t_{irr}/\tau} - 1)^{\tau/(\tau-\theta)}$$

With $\alpha$ written out in full, the threshold relation thus reads

$$(e^{t/\theta} - 1)^{\theta/(\theta-\tau)} * (e^{t/\tau} - 1)^{\tau/(\tau-\theta)} = \frac{D_{thr}}{k\tau\theta} \cdot \frac{1+1200\eta_N E}{\eta_B\eta_H E\ (1200\eta_N E+\eta_R\eta_N/\eta_B\eta_H)} \qquad (27)$$

a relation which expectedly reduces to eq. (7) for $\theta = 0$, i.e. when D would behave as C.

Relation (27) is symmetrical in $\theta$ and $\tau$, which means that it gives the same solution, independent of whether we exchange the temporal characteristics of the toxic agent resorption ($\tau$) and of the damage repair process ($\theta$).

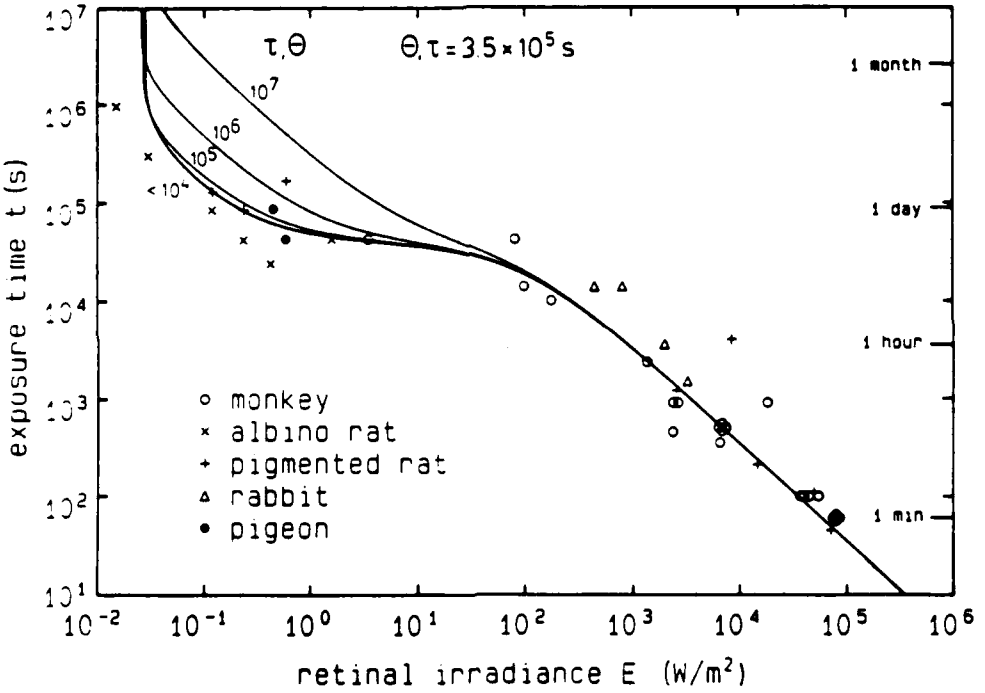


Fig. 4 Calculated retinal light damage relations for various combirations of the toxic agent resorption time ($\tau$) and the tissue repair time ($\theta$). Note that $\tau$ and $\theta$ are exchangeable, so that the curves belong either to $\tau = 3.5 * 10^5$ s and $\theta$ as indicated, or to $\theta = 3.5 * 10^5$ s and $\tau$ as indicated.

The solution of eq. (27) is easy, since for a particular choice of t, the relation is a quadratic equation in E. Fig. 4 gives the solution for a few $\theta$, $\tau$ (or $\tau$, $\theta$) combinations. The original description with $\tau = 3.5 * 10^5$ s (eq. 11) should now be called the $\tau = 3.5 * 10^5$, $\theta \ll \tau$ solution. Typically, the other solutions with $\theta$ comparable to or greater than $\tau$ produce a worse data fit. It is a matter of choice, of

course, whether we interpret the chosen description as a $\tau = 3.5 * 10^5$, $\theta << \tau$ or as a $\theta = 3.5 * 10^5$, $\tau << \theta$ result. All evidence, though, points in the latter direction: it would only be natural to consider the resorption of the toxic agent as a quick process, and the value of $3.5 * 10^5$ s would fit well with the observation that optimal damage diagnosis occurs after some two days. This also clarifies the apparent Kremers/Van Norren vs. Griess/ Blankenstein controversion (see footnote 2).
That means that we can keep the original Kremers/Van Norren description intact, but with a distinct preference to change the attribution of the $3.5 * 10^5$ s time constant from the toxic agent resorption process to the tissue repair process.

## 2.5 Residual damage

All variations on the model, so far, had as a basis that the damage completely disappears for $t >> \tau, \theta$. Of course, this is not entirely realistic since one can assume that some residual effect - in the form of waste products, deposits or scars - will be left. This residual effect will, of course, not be related to $D_{max}$, but rather to the 'damage integral'

$$R = \int_0^\infty D dt$$

We calculate, with eqs (22) and (25)

$$R = \int_0^\infty D dt = k\alpha\tau\theta \int_0^{t_{irr}} \left(1 - \frac{\tau}{\tau-\theta} e^{-t/\tau} + \frac{\theta}{\tau-\theta} e^{-t/\theta}\right) dt +$$

$$+ k\alpha\tau\theta \int_{t_{irr}}^\infty \left[ \frac{\tau}{\tau-\theta} \left(e^{t_{irr}/\tau} - 1\right) e^{-t/\tau} - \frac{\theta}{\tau-\theta} \left(e^{t_{irr}/\theta} - 1\right) e^{-t/\theta} \right] dt$$

With $\tau << \theta = 3.5 * 10^5$ this becomes

$$R = k\alpha\tau\theta \left[ \int_0^{t_{irr}} \left(1 - e^{-t/\theta}\right) dt + \int_{t_{irr}}^\infty \left(e^{t_{irr}/\theta} - 1\right) e^{-t/\theta} dt \right]$$

or, written as a threshold residual damage relation

$$t - 2\theta\,(e^{-t/\theta} - 1) = \text{const} * \frac{1+1200\eta_N E}{\eta_B\eta_H E\,(1200\eta_N E+\eta_R\eta_N/\eta_B\eta_H)} \qquad (28)$$

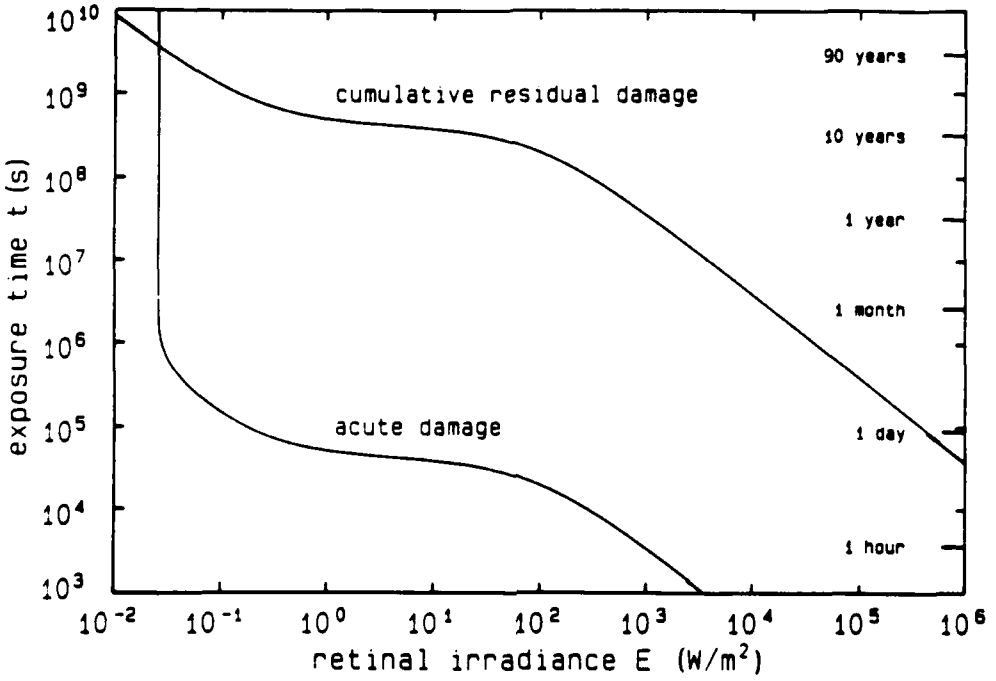


Fig. 5 Hypothesized course of a residual light damage threshold relation, together with the experimentally supported acute damage relation. The cross over is located at about 90 years, the age at which senile macular degeneration is no rare appearance.

The relation shows great similarity with the acute damage relation (7), with the only difference that it resumes its -45° slope for $t \gg \theta$, $1200\eta_N E \ll 1$ due to the absence of complete recovery. We have sketched its course - with a guessed height - in Fig. 5, together with the acute damage threshold course. About the height we can indeed only guess, but we have made that guess on the observation that senile macular degeneration, which sometimes is attributed to chronic over-exposure to bright daylight (Young, 1988), typically is an affliction of very old age. Recent epidemiological evidence seems to support this idea (Muñoz et al., 1990), and we have tentatively located the cross-over at the age of 90 years.

## 2.6 Conclusions

The foregoing sections seem to justify the following conclusions:

- Even after sophistications the Kremers/Van Norren model for retinal light damage remains solidly intact, be it with a better interpretation of the time constant $\tau = 3.5 * 10^5$ s as the tissue repair time.
- The model shows that the acute threshold relation is rather invariant against the type of white light used as irradiant.
- Since the model does not require any unrealistic presumptions one can say that a type of three branch threshold relation should be expected for any animal model. The only difference between species to be expected would be the relative levels of the Noell and the Ham parts.
- A similar reasoning applies to the residual light damage relation. One can expect it at some level because, again, no unrealistic presumptions had to be made. Since signs of residual damage are only observed at high age, the cross over during life time should happen near or above the top of the vertical asymptote.

# 3 CONSEQUENCES FOR OCULAR SAFETY

In particular the invention of the laser has triggered the formulation of occupational exposure standards. Originally these were entirely based upon thermal retinal damage (retinal burn). When it became evident that at a subthermal level photic damage could occur, tentative adaptations appeared to the Threshold Limit Values. It will be clear that the Kremers/Van Norren model discussed in this report, will require further adaptations. These will be discussed in section 3.1. In section 3.2 we will in particular turn to the significance of the model for daily life exposure to bright outdoor light.

## 3.1 Threshold Limit Values (TLVs)

We return to the basic relation (7), or better to its monochromatic version (12). We will now translate these relations to more easily interpretable ocular safety guidelines.

Current occupational health standards specify admissable exposures as a function of wavelength in a somewhat different way, and we therefore have to convert the data of Fig. 3 to enable comparison:

- The data should be converted from ***retinal irradiance*** to ***environmental radiance***. The irradiance (E) to radiance (L) conversion is effectuated by taking into account that the pupil - which can be taken to be constricted to about 2.5 mm diameter at these hight light levels - spans a solid angle ($\omega$) off the retina of about 0.01 sr. That means that

$$L = E / \omega = 100\ E \quad W/m^2\ sr$$

In addition we have to backtransform the data for intraocular transmission losses ($T_\lambda$), so that this conversion should change into

$$L_{env} = 100\ E / T_\lambda \tag{29}$$

By substituting this in eq. (12) we obtain the relation

$$t = -\ 3.5 * 10^5\ \ln \left[ 1 - \frac{1+12\eta_N T_\lambda L}{2.5\eta_B T_\lambda L(12\eta_N T_\lambda L+46\eta_N/\eta_B)} \right] \tag{30}$$

- Then we should, of course, connect these threshold relations to already established ***thermal*** damage safety limits. For these we will take the limits adopted by the Health Council of the Netherlands (1979), which are more closely tied to the experimental damage threshold data than the more common ACGIH limits (1988) which are much more based upon a simple straight line doctrine. Since ***safety*** limits are defined on the basis of a distance of a factor 10 from damage ***threshold*** relations, we have to restore them to threshold level before to do the interconnection. In that way we obtain general retinal damage ***threshold*** relations.

- We should present the relations not in terms of time versus radiance, but in terms of radiant dose Q (i.e. radiance * exposure time, in $J/m^2$ sr) versus exposure time.

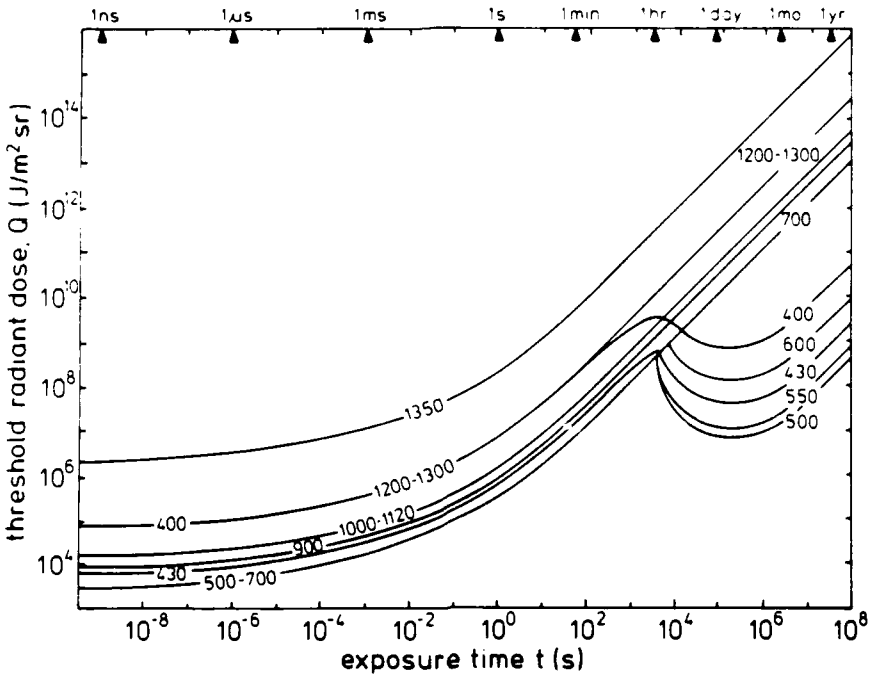


Fig. 6 Threshold Limit Values based upon the Kremers/ Van Norren light damage model, connecting to the Health Council retinal burn TLVs.

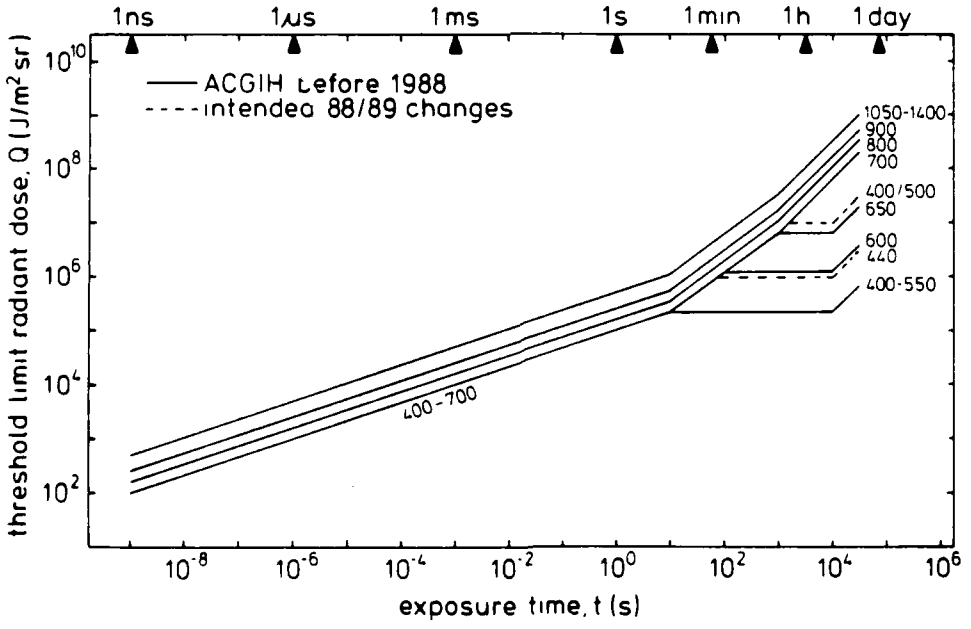


Fig. 7 Threshold Limit Values as defined by the American Conference of Governmental Industrial Hygienists, ACGIH (1988).

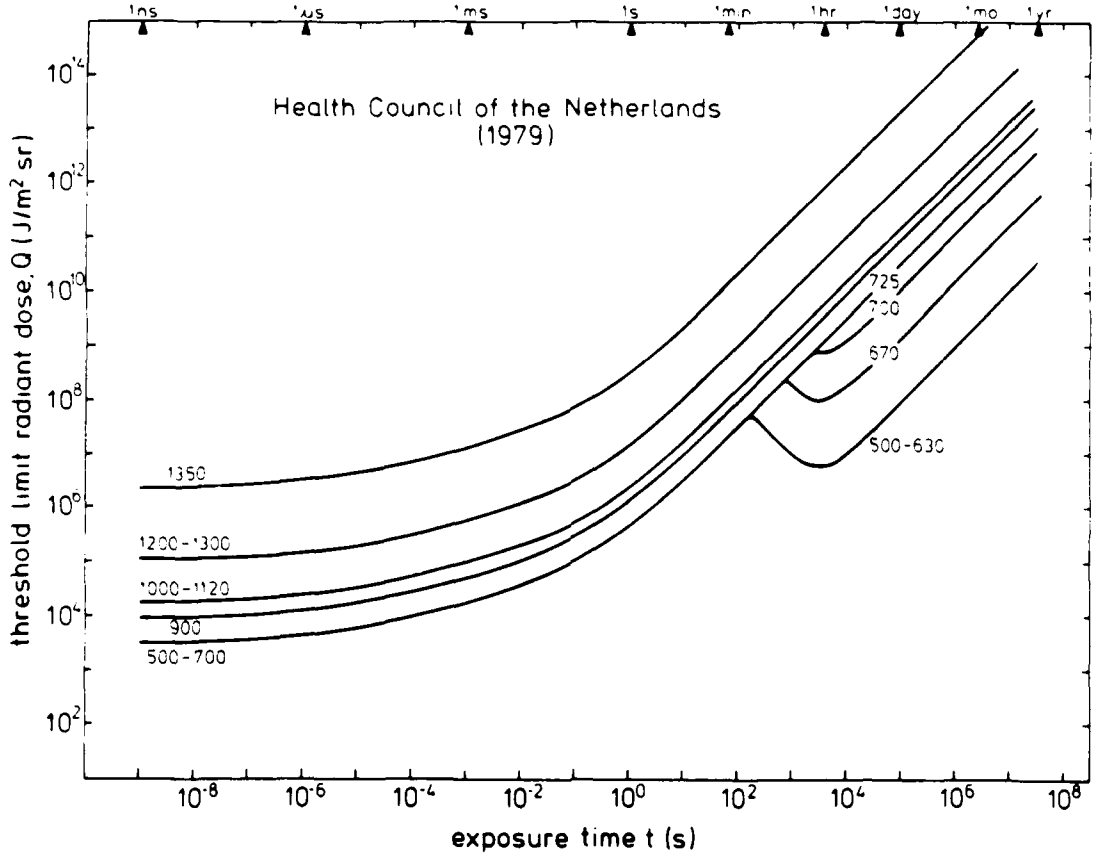


Fig. 8 Threshold Limit Values as defined by the Health Council of the Netherlands (1979).

- Finally we should reapply the safety factor 10 to the whole set of curves. There is an intriguing problem, though. Usually this factor 10 is applied to the intensity scale (E, or Q), but one can easily verify in Fig. 1 that this would lead to a complete absence of a safety margin in the $10^0$ to $10^2$ W/m$^2$ domain, due to the horizontal course. Far better is it to apply a safety belt of a factor 10 in all directions (as illustrated in Fig. 9). Mathematically this is described by a Delation Operation, coming down to rolling a ball of a factor 10 along the threshold relations.

The resulting TLVs are drawn in Fig. 6. These newly suggested TLVs have to be compared with the ACGIH-prescribed relations reproduced in Fig. 7 and with the Health Council relations reproduced in Fig. 8.

The comparison of Figs 6, 7 and 8 induces the following comments:

- The differences between the thermal safety limits of ACGIH and the Health Council were already discussed in the Health Council report

(1979). They seem to mainly due to the straight lines fascination of ACGIH, rather than to basic differences in opinion.

- The in 1979 enigmatical 'dip course' in the photic domain in the Health Council report, is now confirmed and given a theoretical base. However, shape and location appear to be markedly different from the far more hypothetical 1979 TLVs.
- The distance in the minutes to hours domain between the ACGIH TLVs and those derived here is gigantic, in that our TLVs are much higher.
- Of course one may question whether a definition of safe exposure limits for monochromatic light beyond 8 hours is sensible. That question applies already to the hours domain, though. We will leave that matter to decision makers at the policy level and only state that we have provided a tool to calculate TLVs for any light source.

## 3.2 Application to daily life

Certainly more important for daily life is the exposure to bright light which may, already at temperate zones and even more so in the Arctic, extend over hours or even days. We therefore return to Fig. 1 and reinterpret the horizontal retinal irradiance scale in terms of luminance. We base this reinterpretation on the conversion scheme in Fig. 5 in Vos (1966) which features both the luminance and the radiance within the 400-1000 nm window of the human eye, as a function of radiation temperature. We read from it that, at 5100 K (equivalent solar surface temperature at summer altitude in Holland), the sun luminance is $10^9$ cd/m$^2$ and the 'ocular radiance' $5 * 10^6$ W/m$^2$ sr. On the basis of a 0.01 sr pupil size this becomes $5 * 10^4$ W/m$^2$ on the retina. Of course this value has no great accuracy, if only because of the necessarily rough estimate of the pupil size. However, with this transformation rule we can, with reasonable reliability, replot the course of Fig. 1 in terms of outdoor sunlit luminance. This is done in Fig. 9.

In the same figure we have indicated - just like we did before - a safety margin with a width of a factor 10 below which we may take the exposure conditions to be safe with respect to light damage. Moreover we have plotted in this diagram a few representative high light exposure situations, such as all day driving on the road, sailing for a day, flying for hours over a dense sheet of clouds, or observing a solar eclipse during a quarter of an hour.

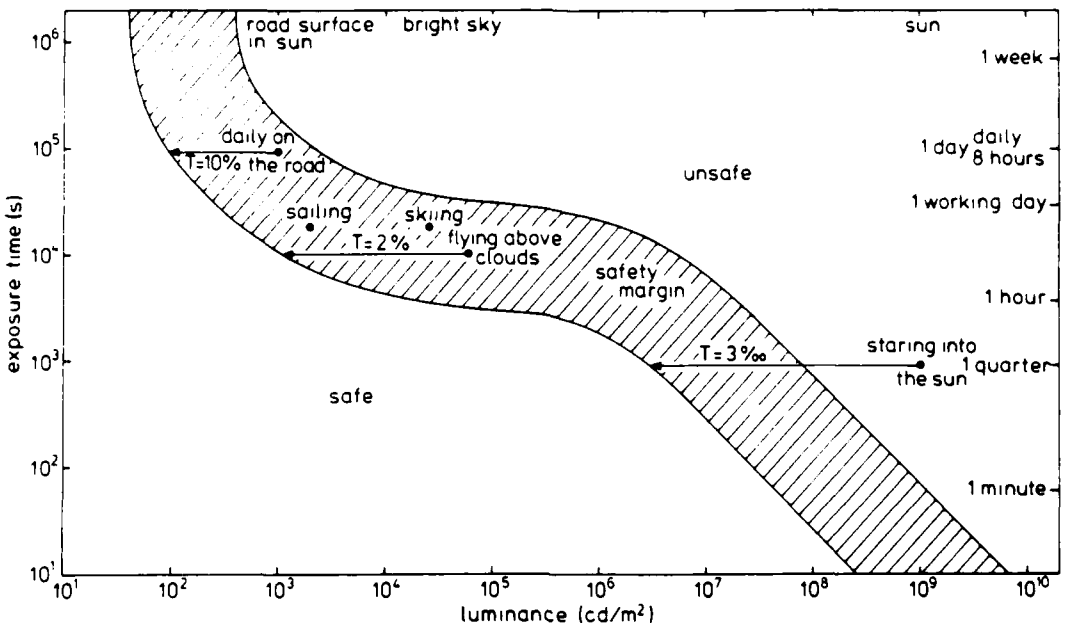


Fig. 9 The time/luminance domain divided in a safe and an unsafe region, separated by a border safety margin of one decade. Arrows indicate the minimum required eye protection by sunglasses.

In this plot the abscissa reads in cd/m$^2$ on the basis of a sunlight spectrum. The distances from the 'situation dots' to the safe border limit are indicated with arrows. The length of these arrows, then, gives the necessary intensity reduction to provide adequate protection; i.e. the necessary density of sunglasses. An intriguing question now is in how far these required densities relate to comfortable densities.

A transmission of 10% (density 1) does not sound unreasonable for professional drivers. True, most sunglasses have lower density, but that is because light leakage around the brims sets a limit to the acceptable contrast between through and around glass light levels (cf. Vos, 1977). Skiers, in approximately the same situation, often wear 10% glasses, but then with side view limitations. A transmission of 3% for pilot visors is a common value indeed. However, a density 2.5 for glasses to observe solar eclipses is far lower than the commonly advised smoked glasses, which may have densitues up to 4 or 5.

One might say therefore that, at these extreme light levels, far beyond virtually complete bleaching, the relation between protection and comfort breaks down. For normal bright outdoor conditions, however, comfort seems to be linkable to protectedness against long term light

damage. This is the first time, to our knowledge, that requirements to sunglasses are directly coupled to possible retinal light damage.

This tentative coupling might have two important consequences. One is that sunglasses may have to be incorporated in a normal occupational health provision package: the professional driver on a sunny day may require sunglasses for protection rather than comfort[3)]. In the second place, we have drawn, as a dotted line, the speculative course of the safe border extension on the basis of residual light damage. Though the cumulative effects of very long term, maybe life long exposure to high light levels are not yet established beyond doubt, light is a likely factor in the development of age-related macular degeneration (Young, 1988; Muñoz et al., 1990). As long as we do not know all the ins and outs, those exposed to the sun, be it for business or for pleasure, might better protect their eyes against this possible chronic effect.

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[3)]This conclusion can only be corroborated, of course, by recent studies on cataract formation by UV (Taylor et al., 1988; Bochow et al., 1989).

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**10. TITLE AND SUBTITLE**

An extension of the Kremers/Van Norren model for retinal light damage and consequences thereof for occupational safety

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**14. SUPPLEMENTARY NOTES**

**15. ABSTRACT (MAXIMUM 200 WORDS, 1044 BYTE)**

The Kremers/Van Norren model gives a comprehensive across species description of retinal light damage threshold as a function of exposure time. It is based upon the assumptions a) that absorption in pigments in retina and pigment epithelium produces a toxic agent; b) that at sub-bleaching light levels the main mediating pigment is rhodopsin; and c) that at supra-bleaching level other pigments, possibly rhodopsin bleach products, take over.
In the first part of this report we have verified the validity of a few silent assumptions in the Kremers/Van Norren model: the neglection of the dynamic nature of the bleach process; the assumption that it is the maximum concentration of the toxic agent that determines the degree of damage; and the assumption that there is no cumulative effect of residual damage. The first assumption proved to be entirely justified. The second one not, but the mathematics of the original Kremers/Van Norren description remain valid when we apply their $3.5 * 10^{5}$ time constant to the repair process, rather than to the toxic agent removal. As to the last assumption, the consequences of a cumulative residual damage mechanism are quantified.
In the second part we have tried to draw consequences for practice. This is done in two ways. In the first place the results of the model computations were converted to convential Threshold Limit Values (TLVs) to make them comparable to current safety standards. It is shown that, on the basis of the model interpretation, these need considerable revision in the long term exposure domain. In the second place the significance is discussed for sunglass prescription. It is shown that requirements for visual comfort run greatly parallel to requirements for ocular safety.

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