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Perspective

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A Perspective on the Ultrafast Photochemistry of Solution-Phase Sunscreen Molecules

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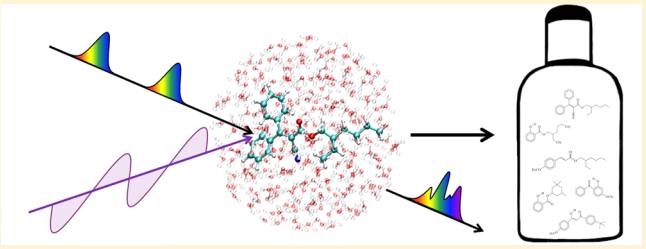
ABSTRACT: Sunscreens are one of the most common ways of providing on-demand additional photoprotection to the skin. Ultrafast transient absorption spectroscopy has recently proven to be an invaluable tool in understanding how the components of commercial sunscreen products display efficient photoprotection. Important examples of how this technique has unravelled the photodynamics of common components are given in this Perspective, and some of the remaining unanswered questions are discussed.



Biological systems always exist in some sort of equilibrium, where both too much or too little of something adversely effects the chance of survival, a so-called *burden of disease*. Plants, for example, require sunlight for photosynthesis in order to provide energy for metabolism, but too much can damage photosynthetic machinery and even increase susceptibility to invading pathogens.[1,2] Humans are of course no exception to this rule, where such a burden of disease exists for a myriad of physical and biochemical variables. One prominent example of this is with ultraviolet radiation (UVR; 400−100 nm) exposure,[3,4] where UVR is typically subdivided into three regions, UV-A (400−315 nm), UV-B (315−280 nm), and the most energetic region, UV-C (280−100 nm). Given the ozone-rich atmosphere of the Earth, high-energy components of the incident solar spectrum are absorbed and scattered before they reach the surface of the Earth. The result is that all UV-C components are absorbed and scattered, and the resultant terrestrial solar spectrum is composed of much less than the ∼8% UVR of the solar spectrum.[5] This small portion of ultraviolet light has far-reaching consequences for the terrestrial biosphere.

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Positive Effects of UVR Exposure. Probably the most well-known positive attribute of UVR exposure involves UV-B radiation in the production of vitamin D. More than 90% of the vitamin D requirements of the body are met through the UV-B-mediated conversion of 7-dehydrocholesterol to previtamin D_3.[6,7] Furthermore, a deficiency in vitamin D has been associated with rickets and skeletal disease, particularly in the early development of bones in children for example.[6,7] Adequate vitamin D has also been linked to a reduction in the incident rates of other diseases such as some cancers, for example, non-Hodgkin's lymphoma and breast cancer, as well as some psychiatric disorders such as schizophrenia.[3,4]

Negative Effects of UVR Exposure. Without doubt, the most prominent effect of UVR overexposure is the development of skin cancers, both nonmelanomas, such as basal and squamous cell carcinomas, and malignant melanomas.[4,8] In fact, UVR exposure is the root cause in the development of skin cancer in an estimated 80−90% of cases in Europe, North America, and Australia,[3,9] contributing to the ∼55 000 worldwide fatalities annually.[4] UVR exposure has also been linked to various other disease burdens associated with skin, for example, premature skin-aging and photodermatoses, as well as other UV-sensitive tissues such as the eyes, for example, cataracts of which there are around 3 million cases globally per annum.[4] Indirectly, UVR exposure also contributes to the global disease burden by disrupting the immune system. In this way, UVR can interrupt and suppress cell-mediated immunity, leading to an increased susceptibility to invading pathogens. A summary of the common ailments from UVR under- and overexposure is summarized in Figure 1A.

Most of these problems are linked to the chromophores of DNA, that is, nucleobases, which are strong UV absorbers. Skin-penetrating UVR leads to changes in molecular electronic configurations, manifesting in changes in the molecular structure either directly, for example, new chemical bonds forming, or indirectly, through the generation of free radicals.[13] In response to this, the body has evolved a fascinating and

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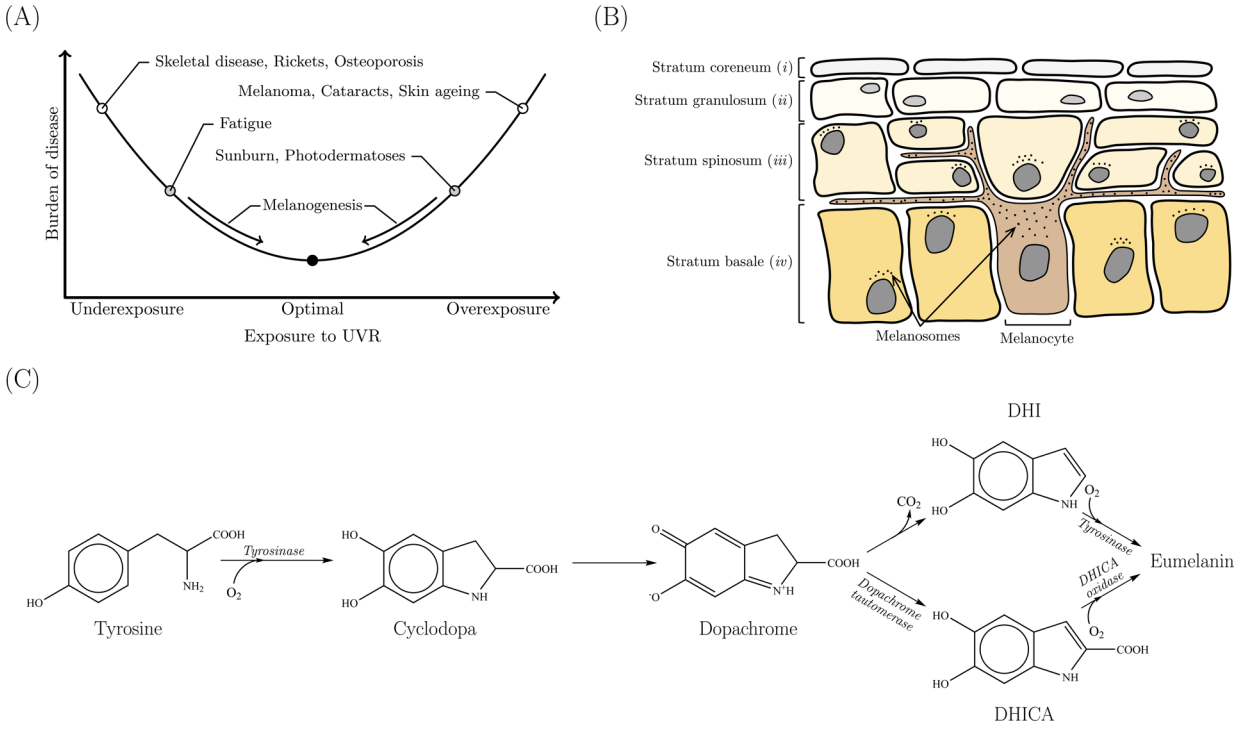

Figure 1. (A) Burden of disease curve, representing the probability of disease incidence as a function of UVR exposure, highlighting some of the common acute (gray circles) and chronic ailments (white circles). Melanogenesis can be up-regulated (down-regulated) in response to increased (decreased) UVR exposure to perturb the burden of disease toward an optimal position, with the lowest incidence of disease. (B) Schematic representation of the different layers found in the skin epidermis. (*i*) The stratum coreneum is a protective layer of dead keratinocytes. (*ii*) The next layer, the stratum granulosum, consists of keratinocytes that migrate toward the stratum coreneum and in the process lose their nucleus. (*iii*) The thickest layer of the epidermis, the stratum spinosum, is packed with keratinocytes. (*iv*) The bottom-most layer of the epidermis, the stratum basale layer, consists of both keratinocytes and melanocytes. These melanocytes synthesize melanosomes, which are melanin-containing membrane-bound organelles. Through a variety of complex processes,[10,11] melanosomes are then distributed throughout the basale and spinosum layers and form a supranuclear cap to the nucleus of surrounding keratinocytes, protecting DNA from incoming UVR. (C) Melanins and, in particular, eumelanin are synthesized in melanosomes through a tyrosine-driven biochemical pathway, where the main steps are shown.[12] The final photoprotective eumelanin is a polymer consisting predominantly of 5,6-dihydroxyindole (DHI) and 5,6-dihydroxyindole-2-carboxylic acid (DHICA). Parts of this figure are adapted with permission from ref 16.

complicated set of processes to deal with DNA damage. (i) DNA damage recognition and checkpointing are capable of identifying damage in a cell, which can initiate an appropriate response. (ii) DNA repair mechanisms, which attempt to rectify damage or, in the case when damage cannot be repaired, initiate apoptosis to stop a damaged genome from replicating.[14,15] These mechanisms are however not perfect, and cells with these mutations can divide, which can lead to cancer. Therefore, reducing the likelihood of UVR damaging DNA in the first place should be considered a primary photoprotective mechanism, for humans; this is achieved through skin pigmentation.

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Natural Photoprotection: Melanins. Natural skin pigmentation involves a class of UV-absorbing molecules, termed melanins, that are capable of capturing harmful UVR and dissipating it through less damaging photophysical processes, such as conversion to thermal energy. The two main classes of melanins are eumelanin, a black-brown pigment, and pheomelanin, a yellow-reddish pigment. These melanins provide photoprotection through skin pigmentation (predominantly eumelanin) and are synthesized in specialized cells called *melanocytes*, which reside in the stratum basale layer of the skin epidermis; see Figure 1B. Eumelanin is synthesized through a tyrosine-driven biochemical pathway, where predominately 5,6-dihydroxyindole and 5,6-dihydroxyindole-2-carboxylic acid are polymerized together to form long chains, briefly summarized in Figure 1C.[12] Eumelanin is packed inside membrane-bound organelles called *melanosomes*. Melanocytes distribute melanosomes to the surrounding skin keratinocyte cells via a network of dendrites (branches of the melanocytes) and a series of cytoskeletal-assisted processes.[10] The melanosomes enter the cells and form a supranuclear cap, which significantly reduces the probability that incident UVR penetrates the nucleus, thus limiting damage to DNA. Overall, the degree of photoprotection will depend on the size and distribution of melanocytes,[16] as well as the concentration of eumelanin inside of the melanosomes themselves, properties that are controlled and regulated via a set of genes.[15,17] It is with these genes where skin pigmentation becomes dynamic; in regions of high UVR exposure, more than the skin is currently protected against, these genes are up-regulated to increase skin pigmentation, often referred to as facultative skin color or, "tanning".[10]

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Conversely, when UVR exposure is too low, these genes can be down-regulated and facultative skin color is lost. Collectively, this gene response for skin pigmentation is referred to as the process of *melanogenesis*. It is through this process that the body dynamically responds to environmental UVR levels as well as metabolic requirements in order to maintain an optimal position in the burden of disease. There is however a problem with melanogenesis; while additional pigmentation will lead to a greater degree of photoprotection, it is a delayed response, typically occurring ∼3−5 days after UVR overexposure, where any intermediate response provides essentially no additional photoprotection.[18,19] Thus, photodamage may have already occurred by the time the body has begun to respond to damaging UVR levels.

Artificial Photoprotection: Sunscreens. Given the growing availability for travel and tourism,[20] as well as the current trend in a favorable attitude to sun bathing and tanning,[19] people are becoming increasingly subjected to UVR levels beyond which their natural photoprotection prepares them for. Fortunately, there are a number of solutions to this problem, the most simple being to avoid UVR overexposure, for example, seeking shade around the solar meridian, wearing additional attire, and the use of sunscreens. Given current trends and attitudes, the latter has almost become the universally preferred option for many people worldwide.

Sunscreens are applied to the upper epidermis of the skin and reduce the density of UVR that reaches deeper UV-sensitive tissues, through both absorbing and scattering UVR. *Organic filters* are usually aromatic molecules that absorb UVR and dissipate the energy through nondestructive pathways (often as heat). *Inorganic scatterers* on the other hand absorb as well as scatter UVR away from sensitive tissues.[21−23] Together, organic filters and inorganic scatterers can provide broad spectral coverage across all damaging wavelengths of UVR, which is the primary rationale for commercial sunscreen products. However, further considerations are taken when designing such products, for example, the color, texture, smell, and ease of application are important; otherwise, the end-user might not continue to use and reapply the product, and thus, protection quickly diminishes. For this reason, a typical sunscreen product contains tens of components in order to produce an efficient, broad-band photoprotective, and aesthetically pleasing mixture.[24,25]

A problem remains however. These rationale do not necessarily lead to a biologically safe product. For example, if a sunscreen component dissipates energy through destructive pathways, then radicals might form which themselves can damage tissues, or if radiative pathways exists, the ejected energy is capable of damaging surrounding cells. This uncertainty highlights the "sunscreen controversy", which asks the question: do the components of sunscreens adversely effect the physiology of the body?[26,27] For example, some components have come under scrutiny as potential endocrine disruptors, sources of free radicals, and a cause of contact dermatitis.[28] For this reason, there are usually regulations on the maximum concentration of any one particular molecule used in a commercial product.[26]

It is here where ultrafast photochemistry is beginning to contribute to the resolution of the sunscreen controversy. By understanding the detailed photophysical and photochemical processes that a sunscreen component undergoes at the molecular level, an evaluation on its photosuitability can be made. Furthermore, solution-phase measurements of these components, as opposed to isolated gas-phase measurements, are a step closer to mimicking the environment of a commercial sunscreen. The remainder of this Perspective is composed of the following: first, the popular experimental approaches to studying these types of systems are discussed, and then, the current state of the literature is reviewed, with examples focusing on specific classes of widely used sunscreen molecules. Finally, we highlight some of the remaining challenges in designing sunscreens from a "bottom-up" approach.

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In order to unravel the relevant dynamics, one must use techniques that can resolve these ultrafast processes.[29,30] In ultrafast spectroscopy, laser pulses, with a time duration on the order of 100 fs (1 fs = 10^{-15} s) or less, are used in a pump−probe scheme (Figure 2). The pump pulse excites a portion of the sample molecules and provides initiation of the photochemical process and thus the start of the experiment. At a discrete time later, a probe pulse interacts with the sample, and in measuring this probe, we garner information about the

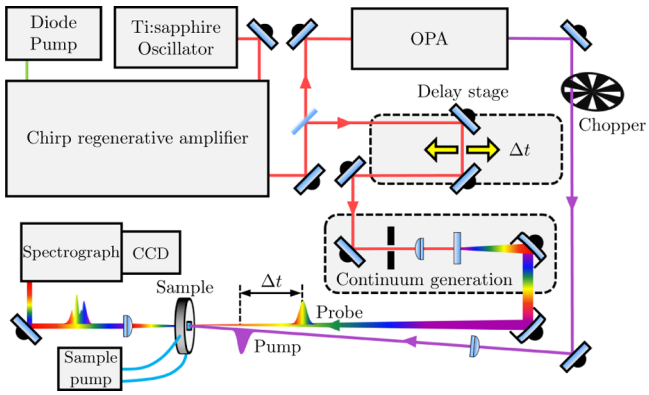

Figure 2. Schematic diagram of a typical transient absorption setup.[32] Essentially there are three stages. (i) Ultrafast pulse generation: A mode-locked Ti:sapphire 800 nm oscillator seeds a chirp regenerative amplifier where pulses are stretched temporally before being amplified and finally recompressed, producing ∼45 fs, 1−3 mJ·pulse^{-1} pulses at a typical repetition rate of 1 kHz. (ii) Pump−probe setup: The 800 nm output is split into two beams; one seeds an OPA that provides the pump pulses, and the other seeds the continuum generation stage, producing probe pulses. A delay stage provides a time delay between pump and probe pulses and can be placed in either beam path (here shown in the probe path). (iii) ΔOD measurement: Pump and probe pulses overlap inside of the sample cell, and the optical density of photoexcited molecules compared to their ground state is measured as a function of time delay and probe wavelength; the result is a differential absorption spectrum, $\Delta OD(\lambda,\Delta t)$.

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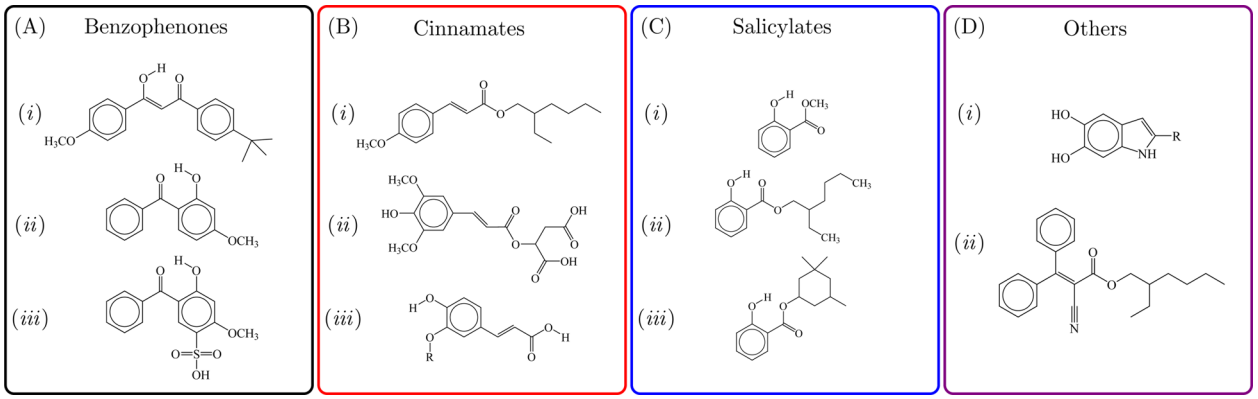

Figure 3. Common sunscreen organic filters. (A) Benzophenones: (*i*) avobenzone, (*ii*) oxybenzone, and (*iii*) sulisobenzone. (B) Cinnamates: (*i*) octyl methoxycinnamate, (*ii*) sinapoyl malate, and (*iii*) ferulic acid (R = CH_3) and caffeic acid (R = H). (C) Salicylates: (*i*) methyl salicylate, (*ii*) octyl salicylate, and (*iii*) homomethyl salicylate. (D) Others: (*i*) 5,6-dihydroxyindole (R = H), 5,6-dihydroxyindole-2-carboxylic acid (R = CO_2H) and (*ii*) octocrylene.

system for that particular pump−probe time delay (Δt). Undoubtedly, the most widely used pump−probe scheme is transient absorption, where, following excitation, the change in the sample absorbance is recorded over time. Changes in the intensity of particular probe wavelengths across time can display characteristic signatures of transient species and excited states, for example, ground-state bleach, excited-state absorption, stimulated emission, and photoproduct absorption. Various pump and probe energies may be used to provide for different problems. In many cases, one is concerned with excited electronic state lifetimes; therefore, the pump pulse is in the UV/visible region. These excited electronic states are commonly probed with either UV/vis pulses in transient electronic absorption spectroscopy[31−33] or infrared (IR) pulses for transient vibrational absorption spectroscopy,[34,35] depending on what chemical information one requires, the former being electronic changes and the latter vibrational information.

A schematic of a typical transient electronic absorption spectroscopy experimental setup is shown in Figure 2. Simply, it comprises an ultrafast laser system, light conversion, delay generation, sample delivery, and probe detection. Broad-band UV/vis probing is facilitated by (white light) continuum generation in various media such as sapphire, CaF_2, and water; the chosen medium and seed energy dictate the spectral range and shape of the generated continuum. For variable pump energies, an optical parametric amplifier (OPA) may be used. These can typically produce energies in the region of 250−1000 nm. The pump−probe time delay is generated using a couple of paired mirrors or a retroreflector on a motorized translation stage. Various sample deliveries may be used, from a simple static cell to a liquid jet; more frequently, though, a flow-through cell of some type is used to ensure that a fresh sample is present for each laser shot. Finally, a spectrograph combined with a silicon-based array detector, such as a charge-coupled device (CCD), records the probe intensities for each time delay. A mechanical chopper in the pump beam, tuned at half of the repetition rate of the laser, allows the probe to view a pumped and then unpumped sample sequentially. Calculating the difference of these pumped and unpumped shots yields the change in absorbance, commonly given as ΔOD (optical density).

For transient vibrational absorption spectroscopy, the same scheme is used, but in place of white light generation, another OPA is needed to generate IR probe pulses, generally in the region of 1250−4000 cm^{-1}. The entire IR beamline must be enclosed and purged with dry nitrogen to avoid absorption from atmospheric H_2O and CO_2. Detection of the IR probe is typically achieved using a nitrogen-cooled mercury cadmium telluride detector.

There are many other techniques in the area that could be useful for studying particular problems, for example, gas-phase photofragment/photoion detection and time-resolved fluorescence. While gas-phase studies[36,37] can be particularly fruitful in the understanding of photodegredation pathways, they cannot capture important environmental perturbations such as solute−solvent and solute−solute interaction, and while cluster studies are capable of providing some of this information, they still remain limited. Time-resolved fluorescence with setups using optical Kerr gating[38,39] or up-conversion[40,41] can also be highly complementary, in particular, to transient absorption spectroscopy.

We now turn our attention to prominent examples of the main families of sunscreen molecules that are used to provide broad spectral coverage across the UV-A and UV-B regions in commercial products (see Figure 3), many of which have been studied using transient absorption spectroscopy.

Benzophenones and Derivatives. These are a class of molecules that contain two aromatic rings connected by a carbonyl group; see Figure 3A. They are used widely as organic UV-A and UV-B filters due to their strong absorption in these regions, usually via strong absorbing $^1\pi\pi^*$ transitions. (*i*) Avobenzone has been widely used in commercial sunscreens since the 1970s and, as such, has been the subject of numerous studies. It exhibits a broad-band absorption maximum in the UV-A region, ∼350 nm, which extends into the UV-B region, peaking again at around 270 nm,[42] and exists in an energetically preferable enol tautomer, as shown in Figure 3(A)(*i*).[43,44] Through nanosecond flash photolysis experiments, avobenzone has been shown to relax through an enol−keto tautomerization.[42,46] Recently, Dunkelberger et al. performed transient electronic absorption measurements on avobenzone in a series of solvents to understand the relaxation mechanism on the ultrafast time scale.[45] Exciting avobenzone at 350 nm populates the first excited state, S_1, which promptly decays over ∼0.4−1.4 ps, depending on the polarity of the solvent, and forms an ensemble of energetic populations, a chelated enol−avobenzone and three distinct nonchelated enol−avobenzone isomers,[45,47] the relative proportions of which depend on the solvent, in the

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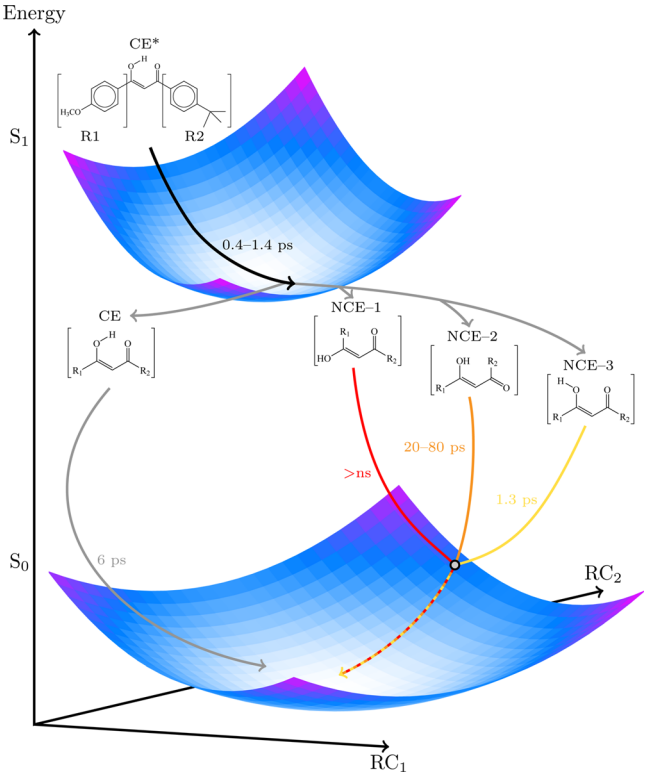

Figure 4. Representative schematic of relaxation pathways exhibited by avobenzone along some reaction coordinates (RC_1 and RC_2) as suggested by Dunkelberger et al.[45] After 350 nm photoexcitation, the chelated enol isomer (CE*) is formed in the S_1 state. This isomer relaxes into the ground state, S_0, forming a vibrationally hot enol isomer (CE) or one of three nonchelated enol isomers (NCE-1/2/3), all of which have different relaxation lifetimes, as described in the main text.

ground state, S_0; see Figure 4.[48] The vibrationally hot chelated enol−avobenzone re-forms the ground-state enol−avobenzone state by ∼6 ps through vibrational energy transfer to the surrounding solvent. The nonchelated structures have quite different relaxation time scales; one re-forms the ground enol−avobenzone by ∼1 ps, the second remains for ∼20−80 ps, while the third extends beyond the time duration of the experiment. The incomplete recovery of the ground-state bleach suggests that some of enol−avobenzone transforms into the keto isomer, as inferred from other measurements.[42]

(ii) Oxybenzone, for similar reasons to avobenzone, has found widespread use in commercial sunscreens due to a strong absorption cross section across the UV-A and UV-B regions, exhibiting broad peaks at ∼325 and 287 nm, respectively. There have now been several studies focused on understanding the ultrafast photochemistry that oxybenzone displays after UV excitation.[49−53] Ultrafast (electronic and vibrational) transient absorption measurements have been able to suggest an almost complete relaxation mechanism.[50,51] Oxybenzone exists in an energetically more stable enol isomer that, after 325 nm photoexcitation, predominately populates the $S_2(1^1\pi\pi^*)$ state. This relaxes by internal conversion (IC) to the $S_1(1^1n\pi^*)$ state and then undergoes an excited-state hydrogen transfer to form a keto isomer, together taking ∼100 fs. A rotation around its aliphatic C−C bond occurs, which allows oxybenzone to couple to its S_0 state through a $1^1n\pi^*/S_0$ conical intersection (CI) on a time scale of ∼400 fs. A ground-state hydrogen transfer and vibrational energy transfer to the surrounding solvent re-forms the enol isomer, which takes place on a time scale of ∼5−8 ps depending on the degree of hydrogen bonding to the solvent bath. An incomplete ground-state recovery suggests that a small portion of the excited-state populations form a photoproduct, which transient vibrational absorption studies attribute to a trans keto isomer from extended C−C rotation,[50] although other studies have suggested that this could be attributed to the formation of a phenoxyl radical.[52] (iii) Sulisobenzone, similar to oxybenzone, was also studied by Ignasiak et al.[52] to reveal ∼700 fs and ∼3−4 ps relaxation components, which may be understood through a radical formation pathway mechanism, similar to one of pathways suggested for oxybenzone.

Cinnamates and Their Derivatives. These are a class of molecules that are derived from cinnamic acid, an aromatic, unsaturated carboxylic acid, which are prevalent as sunscreen molecules in commercial products[21] as well as naturally synthesized in some plants for photoprotection, for example, sinapic acid and sinapoyl malate.[54−56]

(i) Octyl methoxycinnamate has been used extensively in commercial sunscreen products, though surprisingly, literature on its relaxation mechanism from a ultrafast photochemical perspective remains sparse; studies have focused on its stability as an organic filter.[57−59] Studies have suggested that after UV-B irradiation, octyl methoxycinnamate undergoes isomerization from the more stable trans isomer to the less energetically stable cis isomer in both polar and nonpolar solvents.[60,61] Tan et al.[62] have taken further important steps to understanding the ultrafast dynamics of this molecule. Here, they used resonance two-photon ionization to study isolated octyl methoxycinnamate molecules in the "gas-phase", reporting relaxation lifetimes in the nanosecond regime attributed to the population of a long-lived $1^1n\pi^*$ state. Building on this, they used microsolvation with water in order to approximate the solution-phase environment. Interestingly, the addition of this water microsolvation increased the relaxation efficiency remarkably to the picosecond regime due to destabilization of the $1^1n\pi^*$ state, which might otherwise be accessible in the gas-phase environment, although more work remains to be done in order to conclude this.[63] This work laid the foundations of solution-phase studies by Peperstraete et al.,[64] which model octyl methoxycinnamate a step closer to a sunscreen environment. The results indeed suggest that trans−cis isomerization is likely central to the observed photoprotective properties, in contrast to gas-phase measurements.

(ii) Sinapoyl malate is a naturally synthesized molecule in many plants from sinapic acid as part of the phenylpropanoid pathway,[54,55] the plant's equivalent of melanogenesis. This molecule has been suggested to fulfill the role of a sunscreen in plants, where UV-B plays a central role to survival but too much can be damaging.[1,2,29,65] While this molecule is not explicitly used in commercial sunscreen products, it remains a point of interest that might help with the rationale of designing commercial products. Vibrationally resolved gas-phase UV spectroscopy experiments along with steady-state fluorescence measurements by Dean et al.[66] have laid the foundations of understanding sinapoyl malate by chemically deconstructing it into a series of sinapate esters. Their results show that sinapoyl malate is unique in having an inherently broad absorption spectrum even under such jet expansion-cooled gas-phase conditions and likely exhibits an efficient and nonradiative energy dissipation mechanism. Building upon this, solution-phase transient absorption measurements have been able to

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identify the likely underlying relaxation mechanism in a more closely matched environment to how sinapoyl malate is found.[67] After UV excitation (ca. 330 nm), the ground-state trans isomer populates an excited electronic state, which begins to relax. Three components are identified, a short ∼50−600 fs component, a ∼1−5 ps component, and a longer ∼20−30 ps component, depending on the solvent. The study suggests two possibilities for the excited states involved: (I) photoexcitation to a $1^1\pi\pi^*$ state, followed by IC mediated by a $1^1\pi\pi^*/2^1\pi\pi^*$ CI to the $2^1\pi\pi^*$ state. Next, IC along the trans−cis isomerization coordinate follows, which couples to the ground state mediated by a second CI, $2^1\pi\pi^*/S_0$, followed by vibrational energy transfer to the solvent bath. (II) Photoexcitation to the $1^1\pi\pi^*$ state, which couples to the ground state via a $1^1\pi\pi^*/S_0$ CI. For both of these mechanisms, it is suggested that the dynamics occur along a trans−cis isomerization coordinate. (iii) Ferulic and caffeic acids are also naturally synthesized molecules, which also exhibit antioxidant properties,[68] with ferulic acid an already approved organic filter in some countries.[69] The photodynamics have been elucidated and follow closely those discussed for sinapoyl malate.[70] Thus, sinapoyl malate and its derivatives are worthy research candidates for commercial sunscreen products.

Salicylates and Their Derivatives. Salicylates are a group of aromatic esters that have been shown to exhibit enol−keto tautomerization via excited-state intramolecular proton transfer (ESIPT), providing an efficient nonradiative relaxation pathway after UV photoexcitation. Despite their commercial use, many of these molecules have received little attention with respect to their ultrafast dissipation mechanisms. (i) The most well-studied example is methyl salicylate, a subunit of the larger salicylates found in commercial products and thus an ideal model for a bottom-up approach to understanding the photodynamics of the more complex molecules. Methyl salicylate has been suggested to undergo ESIPT after UV photoexcitation in a number of studies over the years, with particular attention on fluorescence properties.[71−80] Herek et al. provided ultrafast measurements in the isolated gas-phase, which identified the ESIPT occurring within 60 fs, as well as a longer decay channel of 120 ps.[81] Solution-phase studies would be an important extension given that fluorescence lifetimes show solvent dependence.[80,82] (ii) Octyl salicylate,[83] and (iii) homomethyl salicylate are often used in sunscreen products, but the literature on their relaxation mechanism remains sparse.[84]

"Others". (i) Indoles, 5,6-dihydroxyindole (DHI, R = H) and 5,6-dihydroxyindole-2-carboxylic acid (DHICA, R = CO_2H). are naturally synthesized subunits of the polymeric eumelanin, responsible for skin pigmentation and thus natural photoprotection.[16,85,86] There has been significant focus on these subunits (and indeed further subunits such as phenol[87−89] and derivatives[90,91]) in an attempt to provide a bottom-up approach to understanding the photoprotective properties of eumelanin. Sundström and co-workers,[92−96] among others,[97−99] have made significant progress in elucidating the relaxation mechanism for DHI and DHICA. Ultrafast measurements have suggested that photoexcited molecules might deactivate through ESIPT in ∼100−200 ps. Furthermore, it has been shown that polymerized units of these molecules deactivate faster, which might contribute to why eumelanin displays such efficient photoprotection.[100] Eumelanin itself has been studied to some extent, but much of its photodynamics still remains to be understood.[100−103]

(ii) Octocrylene is a remarkably popular sunscreen component used around the world.[104] It has found use as an organic filter due to its broad-band absorption profile across the UV-A/UV-B regions,[104] its photostability,[104,105] as well as its properties as a photostabilizer for other molecules such as avobenzone.[105−108] Transient electronic absorption studies have recently been reported.[109] This study highlights the efficacy with which octocrylene absorbs UV-B radiation and deactivates through nonradiative pathways, the majority of which happens by ∼2 ps after photoexcitation. While the exact electronic states that participate in this relaxation pathway remain ambiguous, the dynamical lifetimes extracted are very encouraging for such a widely used sunscreen molecule.

Sunscreen Controversy. There is no doubt that the current state of the sunscreen controversy remains heightened with much literature devoted to highlighting it.[26,27,110−113] Many of the sunscreen filters discussed here have been subject to various studies specifically to evaluate their photostability or effect on the body.[43,104,114−117] For example, oxybenzone, as discussed, predominately relaxes back to its original ground state on ultrafast time scales but ∼10% forms a long-lived photoproduct, where current literature suggests that a trans keto tautomer or a phenoxyl radical are likely candidates.[50,52] These photoproducts, in particular the latter, might go on to cause damage to surrounding cells. Furthermore, the oxybenzone molecules themselves might affect the body through absorption into the bloodstream or even other organisms through sunscreens washing off the skin causing water pollution.[118−120] Knowing detailed spectroscopy about oxybenzone (and indeed other UV filters) has already shown that such adverse effects can begin to be reduced, for example, through microencapsulation, where a filter is embedded inside of a particulate carrier, or through lipid nanoparticles, both of which can reduce the filter−skin interaction and generally improve long-term photostability.[121−127] It is clear therefore that no single field of study is capable of solving the sunscreen controversy alone.

Knowing detailed spectroscopy about oxybenzone (and indeed other UV filters) has already shown that adverse effects of sunscreen components can begin to be reduced.

Outlook. This Perspective began with a general overview of natural photoprotection, cementing the context for the requirement of additional photoprotection, specifically via sunscreen products. Given the propensity for sunscreen use around the world, it is no surprise that they have been the subject of numerous studies, and across multiple scientific disciplines. From ultrafast photochemistry, detailed mechanistic properties can be gleaned from individual sunscreen constituents in the solution-phase, a step closer to a sunscreen environment than the isolated gas-phase. Ab initio calculations can provide strong evidence to interpret the origin of transient signals observed in these experiments. Of particular interest are the transient signals that lie within the temporal resolution of many of these experiments (typically <100 fs), something that quantum dynamic studies can reveal.[53,103,128−130] When extended to include solvent effects, for example, using a

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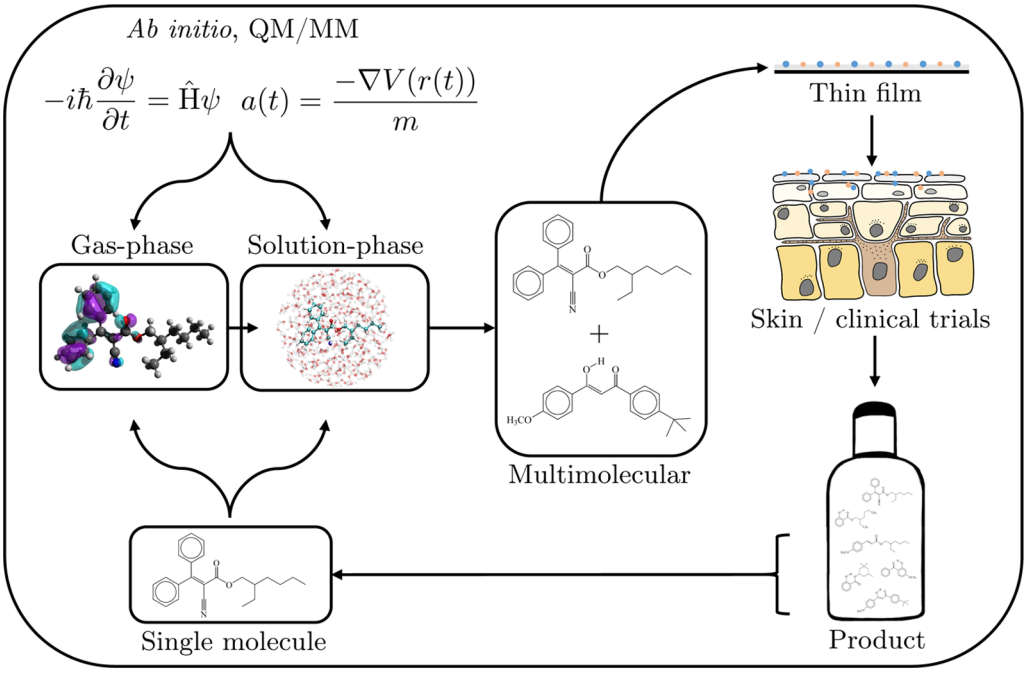

Figure 5. Overview of the proposed process of designing good sunscreen products from a bottom-up approach.[132−135]

continuum solvation model or QM/MM approach,[103,131] these studies can complement solution-phase experiments even more closely.

> From ultrafast photochemistry, detailed mechanistic properties can be gleaned from individual sunscreen constituents in the solution-phase.

We have briefly touched upon the fate of excited-state sunscreen molecules that do not return to the ground state; techniques such as nuclear magnetic resonance and gas chromatography mass spectrometry have shown success in identifying photoproducts.[64,136] However, challenges remain in understanding the photoreactive excited states of these molecules, the formation of radical species, and their subsequent reactions. These processes are often at the root of adverse sunscreen effects. Understanding these processes will enable us to potentially intercept these, thus aiding in the design of novel or improved compounds.

What is being described is a workflow for designing better sunscreens using a bottom-up process; see Figure 5. While we have highlighted a number of important examples of successful sunscreen molecules, there is a long way to go, and it will require interdisciplinary collaboration. A large portion of the Perspective has been focused on solution-phase measurements of unimolecular system, but these studies are often supported and interpreted through gas-phase measurements of isolated systems as well as computational studies. The next step is to introduce multiple components in solution together in order to understand any intermolecular interactions.[137] Following this, one can extend these time-resolved measurements to thin-film studies of creams, pastes, or oils,[138] much closer to commercial products. Finally, skin studies and clinical trials would be required to truly determine the product's safety. At each of these steps, the properties learned feed back into the design of a good component, and thus in a true bottom-up approach using ultrafast spectroscopy, more effective components with well-understood photophysical properties can be selected and used for commercial products.

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Notes

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Biographies

Lewis A. Baker studied Physics at the University of Warwick, obtaining an M.Phys. in 2013. He went on to study Mathematical Biology and Biophysical Chemistry at the University of Warwick Molecular Organisation and Assembly in Cells Doctoral Training Centre, obtaining a M.Sc. in 2014 and proceeding to a Ph.D. with Drs. Vasilios Stavros and Scott Habershon. His thesis focusses on understanding biological photoprotection through transient absorption spectroscopy and quantum dynamic simulations.

Simon E. Greenough completed his M.Chem. in 2010 and his Ph.D. in 2014 in the Stavros group at the University of Warwick, where his thesis focused on an experimental setup for transient absorption studies of photoprotection and photoactivation mechanisms and where he remained for a short postdoctoral position. His current postdoctoral position at the University of Sheffield, in the group of Professor Julia Weinstein, is to implement an ultrafast spectroscopy user facility.

Vasilios G. Stavros is a Reader at the University of Warwick. He completed his Ph.D. in 1999 at King's College London, working in the group of Professor Helen Fielding, and he remained at King's for a further 3 years as an EPSRC postdoctoral research fellow. In 2002, he undertook a postdoctoral position at the University of California

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