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From melanogenesis to melanin technologies

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Melanins are a diverse family of natural pigments with a unique combination of optical, electronic, redox, and structural properties that challenge conventional chemical characterisation. This Perspective summarises key insights from the first international interdisciplinary meeting dedicated to melanin, held in Eastbourne, UK and sponsored by the Royal Society. The meeting brought together advances in melanogenesis, pigment evolution, molecular and supramolecular melanin characterisation, alongside emerging applications in energy storage, sensing, coatings, and biodegradable electronics. Here, we highlight the fragmentation of melanin research across disciplines and advocate for a unified, interdisciplinary approach to understanding melanin's complex chemistry. By integrating perspectives from experts in biology, materials science, paleontology, device physics and chemistry, we propose a roadmap for future melanin research, towards melanin-based functional devices and technologies.

'Melanin' is the generic name for a family of natural pigments generated by the oxidation of tyrosine or other phenolic compounds. Melanins are chemically ill-defined and heterogeneous supramolecular 'polymers', featuring an intriguing set of optical, electronic, redox, antioxidant, magnetic and thermal properties. Melanins defy most traditional chemical characterisation tools: they have less in common with many well-understood biopolymers (DNA, RNA, proteins, glycans), and are far more similar to carbon-based materials characterised by short-range order. Beyond the reach of more standard analyses, understanding melanin's structure-properties represents a considerable challenge.

Due to their biological and medical relevance, as well as their potential as functional materials, melanin research is inherently interdisciplinary and spans chemistry, biology, palaeontology, medicine, materials science and physics, each with its own sub-communities. Nevertheless, melanin researchers have been historically constrained by scientific disciplines, leading to a fragmentation of the field into (i) scientists studying melanogenesis, the chemistry of melanin precursors and melanin mimics; (ii) those focused on melanin as a material, and on leveraging its properties for technological applications; and (iii) those interested in melanin's biological role across diverse organisms.

The Royal Society Hooke Theo Murphy Meeting was organised in February 2024 in Eastbourne (UK) as the first international and interdisciplinary meeting entirely focused on melanin to break these disciplinary silos, prompt discussions, share discoveries and dismantle misconceptions. Attendants were a unique mix of colleagues, many of whom had not met previously, across all career stages and three key domains: melanogenesis and melanin biology, biopigment characterisation and modelling, melanin-based therapies, technologies and devices.

With this Perspective, we aim to report the key topics and challenges that emerged from the meeting of these disparate sub-communities; we also offer a research outlook for the field, promoting a holistic perspective on melanin research.

Melanogenesis and chemistry of melanins

Melanin evolution and function

The evolutionary history of melanins remains largely incomplete, but fossils have begun to provide tantalising insights. Fossil evidence of melanin is known from the Carboniferous (ca. 309 million years ago) to the Neogene (ca. 3 million years ago) in invertebrates such as cephalopods (i.e. ink sac)[1,2] and insects (i.e. eyes)[3] and various vertebrate groups, including cyclostomes[1,4], teleost fish[5,6], amphibians[5,7], terrestrial[7,8] and marine reptiles[9,10] dinosaurs[11,12], pterosaurs[13,14], birds[15,16] and mammals[7,17]. Fossil evidence of melanin includes preserved melanosomes and melanin molecular signatures (McNamara et al.[18], and references therein). In vertebrates, data on melanin type (i.e. relative abundance of eumelanin and pheomelanin), melanosome distribution and abundance, morphology and

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elemental chemistry highlight differences between ectotherm (reptiles and amphibians) and endotherm animals (birds and mammals)[18,19].

The capacity of evolutionarily distant living organisms to synthesise melanins indicates that these pigments are extremely important for life. Indeed, melanins have been proposed[20] as a fourth primordial class of biological polymers that are fundamental for life on Earth, along with nucleic acids, proteins and polysaccharides. Initial roles were probably in homeostasis (e.g. cell regulation) and metabolism (e.g. energy production). Functional diversification of melanin may have been a critical component, if not a driving factor of, major evolutionary transitions, such as the evolution of multicellularity, the transition to life on land, and to homeothermic metabolisms. Integumentary melanin was probably co-opted for visual communication in early multicellular animals over 550 million years ago and remains a striking feature of the phenotype of most animals today.

The Royal Society meeting hosted discussions on how ancient melanin analysis can inform melanin evolution and function across organisms. Despite the taxonomic breadth of fossils reported to have melanin, these are often represented by single specimens or species. Further, melanin has not thus far been reported in fossils of fungi, bacteria and plants; our understanding of melanin evolution remains incomplete.

The functions of melanin in living organisms relate mostly to its abilities to absorb ionising (gamma- and X-rays) and non-ionising (UV, visible, and NIR) radiation and convert it to thermal[21], chemical[22] and electrical energy[23]. This process may also aid in thermoregulation (e.g. cold tolerance in reptiles and fungi)[24–26], enhanced flight efficiency due to enhanced heating of melanised wings in birds[27] and increased ATP consumption (and thus metabolism) in fungi[22]. The ability of melanin to scavenge free radicals also strongly contributes to its role in photoprotection and heavy metal sequestration (see Section 'Melanin metallome')[28].

An additional and obvious function of melanin is in coloration. Melanin pigmentation directly produces black, brown, grey and rufous colours in vertebrates, plus iridescent and non-iridescent structural colours (many with a UV component) where melanosomes are organised into, or serve as a backing pigment to highly ordered, optically active nanostructures[29] in the feathers of birds and non-avian dinosaurs[30]. The rich avian colour gamut reflects, in part, the diverse geometry and structure of avian melanosomes, which can be oblate, hollow, or porous, in addition to the solid spherical and prolate (ovoid) geometries present in other organisms. The development of these unique melanosomes during feather development remains mostly unknown[31–33]. Melanosome shape is dictated by the arrangement of internal amyloid protein fibrils during development, and differs for different melanin pigments[34]. How are different melanins distributed within individual melanosomes and how does this vary with melanosome shape, in different tissues and taxa? Answering these questions requires a molecular-level characterisation of melanosomes from diverse tissue sources and manipulation of gene expression in cultured melanocytes. This will provide enormous insight not only into these genetically modified organelles but also into the development of more typical melanosomes, about which much remains unknown. It may also inspire new synthetic methods for biomimetic melanosomes for structural colour applications, which have thus far been limited to platelet-shaped[35] and 'inverse' synthetic melanosomes with melanin cores and silica shells[36].

Melanin classification and melanogenesis

Melanins are a class of pigments found across the tree of life[37]; they are synthesised in vivo by diverse organisms, such as fungi, microbes[38], plants[39] and animals[40,41] using different molecular precursors[20] (see Fig. 1). Since Berzelius first used the term 'melanin' in 1840 to classify the dark pigments from the eyes of animals, five widely recognised melanin classes are[42]:

Eumelanin (brown to black, insoluble): Eumelanin occurs in mammals, fish, cephalopods, amphibians, birds, insects, reptiles, fungi and bacteria[1,7,43,44]. It is formed via the oxidative coupling of 5,6-dihydroxyindole (DHI) and 5,6-dihydroxyindole-2-carboxylic acid (DHICA), which are biosynthesised from L-tyrosine by a tyrosinase-mediated oxidation[45].

Pheomelanin (red to yellow, slightly soluble in alkali): Pheomelanin occurs in mammals, fish, amphibians, reptiles and birds, insects[46] and plants[1,7,44,47]. Like eumelanin, it derives from L-tyrosine but incorporates L-cysteine at an early stage of biosynthesis, by addition of L-cysteine and dopaquinone. The resulting cysteinyldopa is then transformed into benzothiazine and benzothiazole derivatives before further oxidative coupling[48].

Neuromelanin (brown to black, insoluble): Neuromelanin is the dark pigment produced in neurons e.g. of the *substantia nigra*. It is suggested to have a core-shell structure, comprised of a pheomelanin core and a eumelanin shell[49]. Within the brain, neuromelanin is biosynthesised from dopamine, cysteine and DHI[49], and is associated with lipid and protein matrices[50] and with metal ions (e.g. Fe^{3+})[51].

Allomelanin (brown to black, insoluble): Allomelanin are nitrogen-free pigments found in plants and fungi[39,52,53]. In plants, allomelanin is biosynthesised by oxidative coupling of catechol and catecholic acids (i.e. caffeic, chlorogenic, protocatechuic or gallic acids). In certain fungi, polymerisation involves 1,8-dihydroxynaphthalene (DHN), a metabolite biosynthesized via the polyketide pathway, and is initiated by laccases.

Pyomelanin (light-to-dark brown, sparingly soluble): Pyomelanin occurs in various bacteria (i.e. *Legionella pneumophila, Pseudomonas aeruginosa, Shewanella algae*). It is biosynthesised via laccase-mediated oxidative coupling of homogentisic acid (HGA), an intermediate in the metabolism of L-tyrosine[54,55].

While this classification system is widely adopted, multiple melanogenic pathways can occur in concert, such that some living organisms can produce more than one type of melanin pigment. Hybrid melanins can also be produced from the oxidative coupling of two or more monomers[56,57].

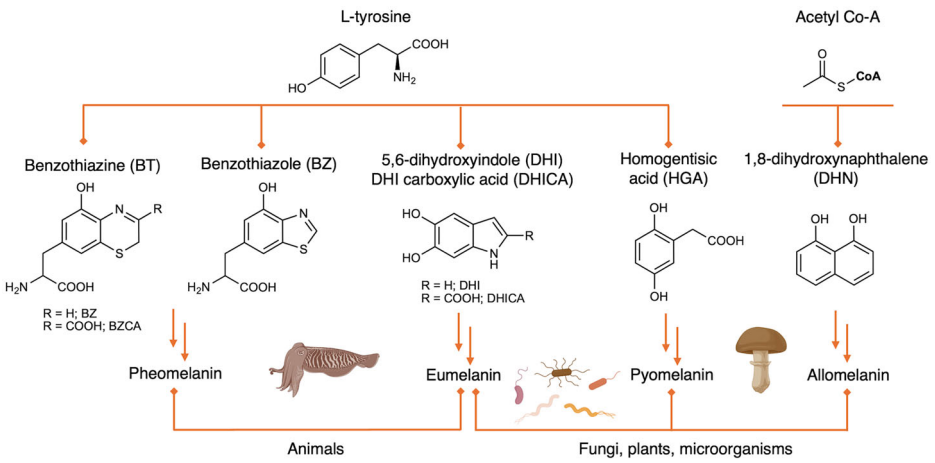

Fig. 1 | Melanin classification and precursors. Melanin classification, molecular precursors and associated organisms. Created in BioRender. Matta, M. (2025) https://BioRender.com/abl32gf.

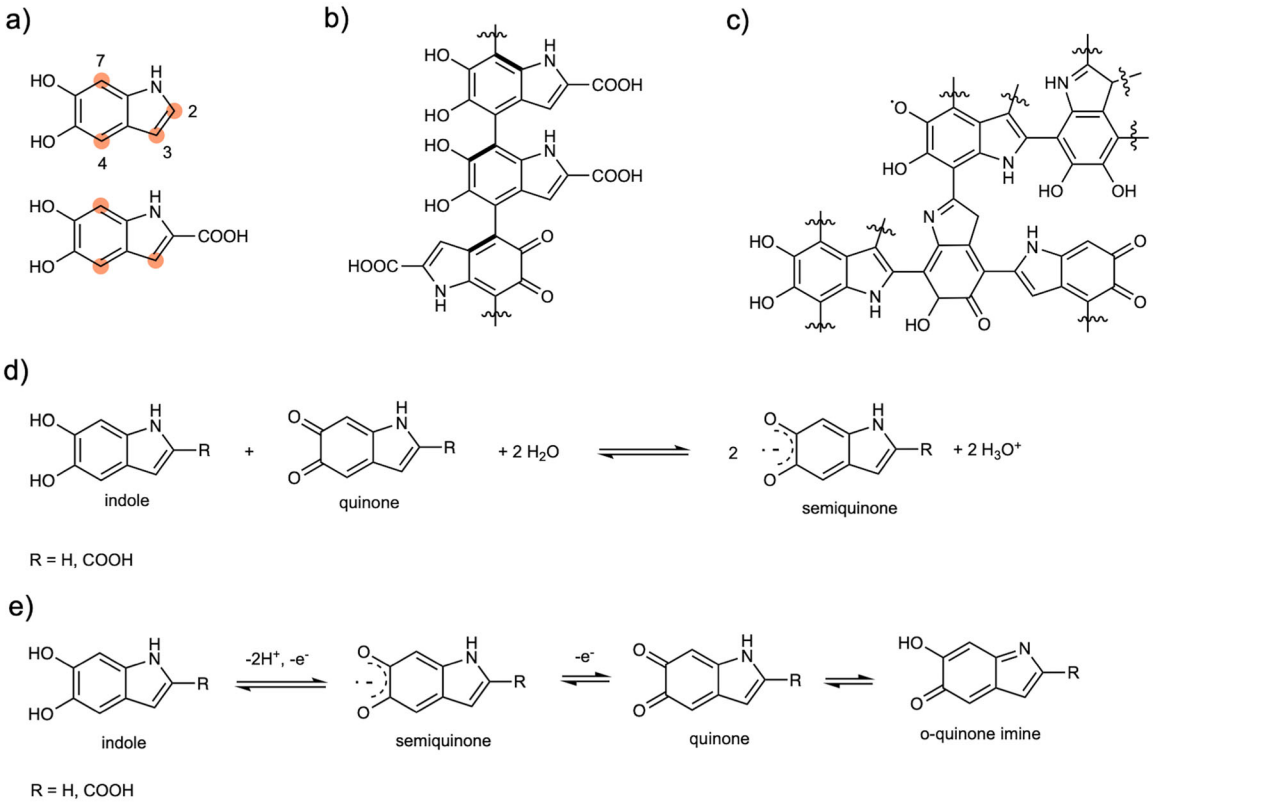

Fig. 2 | Eumelanin's reactivity, structural and redox disorder. a Reactive positions of DHI and DHICA; connectivity patterns in **b** DHICA-rich domains and **c** DHI-rich domains; **d** comproportionation reaction; **e** redox forms and tautomers.

In addition to this, many natural melanin monomers can be produced synthetically (including all in Fig. 1), or by enzymatic conversion of tyrosine, and synthetic melanins can be produced by oxidative coupling — mediated by atmospheric oxygen, or chemical/enzymatic oxidants – of these and other monomers (notably, dopamine)[58]. These 'synthetic melanins' can reproduce some of the properties observed in biologically derived materials (namely, broadband absorption) and are studied both as functional materials and models for natural melanins[59].

Molecular and supramolecular structure

A pressing and persistent challenge facing melanin science is the elucidation of its molecular structure. Unlike other biomaterials or biopolymers, while the molecular precursors of different melanins have been identified, their chemical connectivity (see Fig. 2a–c), and the resulting functional subunits which give rise to the hallmark properties of melanin, are not well understood. The literature often refers to melanins as 'polymers'; however, other sources suggest melanins are not large polymeric molecules, but rather supramolecular aggregates of increasingly insoluble small oligomers[60,61]. Indeed, mass spectra of synthetic eumelanin models (based on DHI and DHICA) reveal oligomeric species up to 30 repeat units[62,63]. Melanin models often reduce this structural complexity to a single cyclic tetramer[64,65] (although this species has not been isolated)[66]. Others consider melanins to be large polymeric species, and researchers have observed spectra of very high molecular weight species (30–175 kDa)[62,67] from samples of eumelanin. This diversity of opinion may arise from the structural diversity across melanins, or from the lack of robust and consistent analytical methods[62,68].

While molecular structure remains opaque, we have some insight on melanin's supramolecular structures. This assembly is difficult to study without isolating the constituent molecules (though some observations are possible, see Section 'Optical and photophysical properties'), but the resulting assemblies have been extensively investigated. Namely, (DHI-rich) *Sepia* eumelanin, which is readily available from cuttlefish ink. Structural characterisation studies via X-ray scattering[69], electron microscopy[70], and, more recently, atomic force microscopy[71,72] have revealed how melanin oligomers assemble into hierarchical structures, forming nanoscale aggregates characterised by π-stacking and, most likely, hydrogen bonds. These nm-sized aggregates agglomerate into ~10^{-8} m particles, and, in turn, larger (~10^{-7} m) granules[73]. However, epia melanin differs from the melanin found in vertebrates in both monomer composition and metal chemistry, raising questions about its relevance as a 'fruitfly' model for eumelanin[1].

Biomimetic synthesis and structural characterisation have been instrumental in advancing our understanding of allomelanins[74]. Biomimetic allomelanin can form porous nanoparticles with tunable pore size[75]. Due to the challenges in isolating fungal melanin, it is still unclear whether natural analogues possess similar nanostructure and porosity[76].

Melanin metallome

The metallome (distribution of metal ions) of melanin and melanosomes is increasingly recognised for its role in melanogenesis, chemical reactivity and homeostasis. Melanin biosynthesis is strongly affected by the metal composition and concentration[77,78]. In turn, the metal association depends on the melanin type and pH[79]. For instance, in eumelanin, Ca^{2+} usually coordinates to carboxylate groups, Zn^{2+} coordinates to carboxylate and catechol groups, Cu^{2+} coordinates to catechol groups and $Fe^{2+/3+}$ coordinates to catechol and NH groups[80]. In contrast, in pheomelanin, Zn^{2+} coordinates with hydroxyl oxygen and sulphur; Cu^{2+} binds to carboxylate and quinone imine groups[17].

The biological implications of the melanin metallome are not fully understood, but the discovery that melanosomes in fossil and modern vertebrates are associated with tissue-specific distributions of metals[5,7] strongly suggests that melanin is evolutionarily linked to metal homeostasis. Melanins in internal organs are likely to have a key protective role in the sequestration of toxic metal ions, regulation of redox reactions and metal-mediated biochemical catalysis[18]. Indeed, integumentary melanins have been shown to sequester environmentally-derived metals from metabolic pathways[1,81].

The spatial distribution of melanosome-associated metals, and metal redox chemistry, in fossil animals has applications in the reconstruction of anatomy[7], integumentary coloration[17,81] and phylogenetic affinity of ancient organisms[1]; however, fossilisation has been proven to alter the melanin metallome[5,82].

Melanin structure—properties and characterisation

Characterisation approaches

Melanins are insoluble in most common solvents, and, due to their heterogeneous nanostructure and lack of long-range order, various characterisation techniques (e.g. NMR, single-crystal X-ray analysis or mass spectrometry) have struggled to provide a definitive molecular picture. Moreover, melanins are redox active and responsive to the local microenvironment (e.g. pH, humidity), rendering it difficult to isolate native samples without disrupting the (covalent and/or supramolecular) structure and oxidation/protonation state[42,62].

Two complementary strategies have emerged to address this knowledge gap. The first is based upon a bottom-up approach, in which biomimetic oxidation is stopped at very early time points, before melanisation is complete, yielding small molecules (often soluble) which may then be characterised using traditional analytical methods. These experiments have revealed coupling patterns between monomers and provided some insights into the primary covalent network that links discrete building blocks. However, the small molecules and oligomers that lie along the biosynthetic pathways to melanin are mostly unstable and tend to react further. The spontaneous and largely non-enzymatically controlled formation of melanin pigments, which contributes to their wide taxonomic distribution, makes it difficult to isolate and characterise high molecular weight reaction intermediates[68,83].

The second strategy is a top-down approach that addresses intact melanins, either by chemical digestion[84–87] (partial breakdown of the melanin backbone) to small, analytically tractable, melanin 'markers' or via more modern spectroscopic analyses that can accommodate intact samples. While spectroscopic data from intact melanins are extremely complex, presenting issues with signal deconvolution and interpretation, and strongly affected by the presence of natural matrices associated with the pigment (i.e. keratin, chitin), digestion protocols yield oxidised fragments that can provide only partial and indirect information about relative monomer abundance and chemical substitution patterns, and none about oxidation patterns in the original material.

Overall, the combination of these characterisation strategies is providing an increasingly refined picture of the biosynthetic steps that lead to functional melanins, but substantial work is needed to elucidate the chemistry of the discrete molecular fragments or subunits responsible for melanin-like properties.

Bottom-up approach. The bottom-up approach has investigated the very early stages of oxidative polymerisation, before aggregates begin to form and precipitate from solution. Efforts have been placed on describing the reactivity of monomer precursors to understand the mechanisms of covalent bond formation leading to oligomers. A similar approach has been used for all types of melanin under investigation. Namely, a well-established workflow, consisting of four steps, has been described[88]. These include: (i) oxidative polymerisation of monomeric precursors under biomimetic conditions; (ii) oxidation is stopped within minutes by adding a reducing agent, and treating crude mixtures with acetic anhydride in order to acetylate phenol or catechol functionalities and prevent further oxidation reactions; (iii) deconvolution of complex reaction mixtures using chromatography to isolate pure oligomers; (iv) structural characterisation, e.g. by 1D and 2D NMR spectroscopy and high-resolution mass spectrometry.

Using this approach, it has been possible to examine the different reactivity patterns of the two eumelanin co-monomers, DHI and DHICA. DHI leads to the formation of branched oligomers by forming C–C bonds at the C2, C4 and C7 positions of the indole[88–91], whereas DHICA forms linear oligomers with covalent bonds at C4 and C7 (see Fig. 2a–c). These studies highlight the shared and distinct reactivity of DHI and DHICA, including the role of the carboxylic acid at C2 in biasing the oxidation regiochemistry, also responsible for the different properties exhibited by the resulting melanin polymers[92]. De novo syntheses of DHI dimers[93] and trimers[94] have also provided insights into the reactivity of larger oligomers and their propensity to form covalent bonds, eventually yielding tetramers and even a cyclic pentamer[88,89]. However, these studies have, thus far, failed to provide well-defined compounds that exhibit the characteristic properties of eumelanin, including broadband absorption and radical scavenging[95]. Recently, the synthesis of an oxidised melanin subunit revealed that these properties emerge when the indole core is oxidised[96] (see Section 'Optical and photophysical properties').

A similar workflow has been applied to the study of pheomelanin[97]. During early oxidation stages, 5-*S*-cysteinyldopas lead to the formation of 2*H*-1,4-benzothiazine (BT) and its 3-carboxylic acid (BTCA). Here, too, the carboxylic acid determines the fate of the monomers. Whereas BT yields oligomers characterised by C–C and C–O bonds[98], BTCA forms dimers featuring isoquinoline and benzothiazole heterocycles, plus 2,2′-dibenzothiazines that are rapidly oxidised to trichochromes[99–102].

More recently, studies on the oxidative polymerisation of 1,8-dihydroxynaphthalene (DHN) examined the accumulation of dimers in the fungal allomelanin pathway. The formation of C–C bonds between naphthalene units was localised to the C2 and C4 positions[103,104]. Further studies examining the reactivity of these dimers, prepared in high-yield and large scales by de novo synthesis, highlight the impact of the connectivity of the dimer on the morphology of the final granules. To date, higher-order trimers or tetramers have not been isolated[105]. Finally, pyomelanin formation from homogentisic acid has not yet been addressed by a bottom-up approach, and little is known about its reactivity.

Top-down approach. Since the 1960s, top-down approaches have involved oxidative digestion of native pigments to produce and analyse molecular markers that are secondary reporters of melanin structures. This approach was first reported by Nicolaus and co-workers who used peracetic acid or alkaline permanganate to oxidise eumelanin samples to pyrrole-2,3,5-tricarboxylic acid (PTCA) and pyrrole-2,3-dicarboxylic acid (PDCA)[106,107]. PTCA and PDCA were then used as proxies to quantify the relative amounts of DHICA and DHI present and the branching degree in the native pigment. Using a similar approach, iodic acid treatment was used to yield two pheomelanin markers[108,109] and to analyse both eumelanin and pheomelanin from intact tissues[110,111]. Replacing iodine with alkaline hydrogen peroxide resulted in notable increases in the yields of eumelanin[112] and pheomelanin[111] markers. Simultaneous determination of eumelanin and pheomelanin from tissue samples is possible using alkaline hydrogen peroxide oxidation coupled to HPLC and UV detection[111] and is now possible for additional eumelanin structural markers (pyrrole-2,3,4,5-tetracarboxylic acid, PTeCA; 1,3-thiazole-4,5-dicarboxylic acid, TDCA). The application of this microanalytical protocol to different melanised tissues informs on the biochemical and genetic underpinnings of pigmentation[86]. So far, oxidative digestion studies suggest that PTCA is a specific biomarker for DHICA or 2-substituted DHI units that cleave to afford a carboxylic acid at C2, whereas PDCA is a marker for terminal DHI units, within eumelanin; PTeCA is a marker for cross-linked DHI units also typically found in aged, thermally matured and photodegraded eumelanin.

A new frontier in the top-down analysis of melanin pigments relies on advanced spectroscopic techniques that can be applied directly to melanised tissues or intact synthetic melanins to elucidate structural features. Among these techniques, there has been a particular interest in solid-state NMR[113,114] and Electron Paramagnetic Resonance (EPR)[115], X-ray photoelectron spectroscopy[116], X-ray absorption near edge structure[117], X-ray fluorescence, attenuation total reflectance-FTIR and Raman[118] spectroscopy, mass spectrometry[104] and pump-probe microscopy[86].

Future efforts to determine the structure of melanin should aim to: (i) expand the scope to include the oxidation of homogentisic acid in the pyomelanin pathway; (ii) develop new strategies for the identification and analysis of structural markers of fungal DHN-derived melanin and pyomelanin; (iii) develop a database for collecting spectroscopic analyses for each of the available melanin pigments and tissues; (iv) develop milder digestion-based analyses to extract intact melanin components and oligomers.

Optical and photophysical properties

Melanin photophysics has been of interest for decades because of the photoprotection these pigments provide to organisms through sun screening and the scavenging of reactive radicals. Beyond these important biological functions, the photoproperties of melanins, such as broadband absorption and semiconductor-like behaviour, further drive interest for energy harvesting and photocatalysis[119,120]. A key to advancing these applications is a greater understanding of fundamental melanin photophysics, and at the Eastbourne meeting, the discussion centred on new results from steady-state and time-resolved spectroscopy.

Fundamental studies of the photophysics of melanin pigments are famously complicated due to the lack of atomistic structural information (see Section 'Characterisation approaches'). The nanoscale structure of melanins, which distinguishes them apart from other small-molecule natural pigments, is critical for understanding their photophysics through optical spectroscopy. Similarly to other amorphous materials, melanin photophysics resides in a space between small molecules and crystalline solids. In the former, excitations are spatially limited and high-level computational treatments are feasible. In the latter, long-range translational symmetry allows for simplified, yet accurate treatments in terms of bands of delocalised states. In melanin and, significantly, in amorphous lab-made organic materials of interest for optoelectronic applications, molecular-scale subunits interact extensively with other units due to their spatial proximity in amorphous, close-packed structures. The oligomers that form melanin nanoparticles define structures built from chromophores, preventing the determination of the limits of individual chromophores. Identifying the interactions among these ill-defined chromophores is essential to understanding the localisation and dynamics of photoexcited electrons in melanins.

Researchers have worked to reach this middle space through bottom-up and top-down studies, respectively, of small molecule mimics and natural and synthetic melanins (see Section 'Characterisation approaches'). An advance presented in Eastbourne is the elucidation of the photophysical properties of a derivative of 5,6-indole quinone[96], a building block of eumelanin[121]. In this derivative, replacing the hydrogen atoms of 5,6-dihydroxyindole (DHI) with bulky blocking groups prevents oxidative polymerisation. Steady-state and time-resolved spectroscopy reveals that the quinone produced by chemical or electrochemical oxidation of the protected DHI derivative is highly stable.

Surprisingly, the blocked quinone mimics several properties of eumelanin. The compound shows broadband absorption that extends beyond 900 nm, indicating a remarkably low transition energy for such a small, closed-shell organic molecule. It also exhibits a sub-picosecond excited-state lifetime, like other highly effective sun screening compounds. The near IR transition is due to a π,π^* excitation centred on the indole quinone core; orbital decomposition analysis shows that the lack of triplet formation is due to an unfavourable energy alignment of the singlet and triplet energy levels stemming from enamine substitution on the ortho-quinone ring. In addition, a 1:1 mixture of the quinone and hydroquinone forms reacts by comproportionation to yield a small, but significant equilibrium population of semiquinone radicals with a eumelanin-like EPR signature (see Section 'Redox activity, charge transport and radicals').

The emergence of melanin-like properties in a small molecule emphasises that suitably oxidised units may be more important to achieving melanin-like properties than extended conjugated domains. It also suggests that melanin-like photoproperties may be achieved by supramolecular aggregation of small oligomer units. The availability of oxidised eumelanin model compounds is an exciting development, offering crucial insights into the molecular-scale emergence of melanin properties where previous fundamental studies only isolated reduced compounds[122,123].

Moving on from bottom-up studies, an understanding of how covalent and non-covalent interactions affect the subunit is needed to understand the emergence of melanin properties. Top-down studies have shown that, despite the existence of discrete groups of chromophores, individual chromophores are strongly coupled to one another[124] and highlighted the important role of chemical heterogeneity[125,126]. Transient spectroscopy experiments reveal sub-ensembles of chromophores that can be selectively addressed by tuning the excitation wavelength[127]. Excitonic interactions among coupled chromophores have been discussed[64], but new models for understanding how photophysical properties are modified by particle morphology and nano- and mesoscale interactions are needed.

There are extensive similarities in the optical response (e.g. UV-vis and Raman spectra) of melanins and of other natural and lab-made carbon-rich nanomaterials, ranging from carbon and graphene quantum dots to natural organic matter, including brown carbon aerosols and dissolved organic matter in terrestrial waterways. A puzzle for the future is to understand the origin of the similar photophysical properties seen in a wide array of organic nanomaterials despite atomic-scale structural differences. For example, bacterial allomelanin and mammalian eumelanin have similar broadband absorption spectra even though the former is nitrogen-free. Combining nano- and molecular perspectives will be crucial for advancing our understanding of melanins and other carbon-based materials.

Redox activity, charge transport and radicals

Redox activity. In eumelanin, the DHI and DHICA building blocks are present in different redox forms: catechol (reduced form), semiquinone (intermediate form) and quinone (oxidised form, see Fig. 2d, e). In aqueous media, the oxidation process is typically dependent on pH and involves the transfer of one/two electrons and one/two protons, corresponding to the various oxidation steps of the catechol motif[128,129].

The synergy between the redox activity of the building blocks and their capability of reversibly binding cations at sites such as the quinone, amine or carboxylic functional groups is a foundation for the use of eumelanin in electrochemical energy storage systems. Fundamental studies carried out by cyclic voltammetry and electrochemical impedance spectroscopy on synthetic and natural eumelanin (*Sepia* melanin) deposited on carbon current collectors revealed its pseudocapacitive behaviour (see Section 'Wound dressing and healing').

Faradaic (redox) processes observable at hydrated eumelanin-metal electrode interfaces under electrical bias, causing the dissolution of the metal electrodes, should not be overlooked when studying the transport physics of eumelanin[130]. The dissolution, enabled by high metal binding affinity of eumelanin and the possible presence of coordinating chloride anions in the eumelanin material, is relevant to the development of environmentally benign resistive switching devices[130].

Charge transport. The electrical properties of eumelanin, characterised by a thermally activated, strongly hydration-dependent conductivity and weak photoconductivity, have attracted scientists since the late 1960s. Electronic band structures analogous to inorganic semiconductors were suggested for eumelanin based on the strong, broadband UV−vis absorption and the π-conjugated molecular structure. After the observation of a reversible resistive switching in eumelanin pellets by McGinness et al. in 1974, electrical measurements on pellets were interpreted within an amorphous semiconductor model[131].

More recently, Mostert et al. demonstrated that the amorphous semiconductor model cannot account for the hydration-dependent conductivity of eumelanin pellets[132]. Instead, in the presence of water, the comproportionation reaction is shifted towards the semiquinone radical and protons, which contributes to charge transport (vide infra)[133]. The

presence of locally mobile protons and free radicals determined by muon spin relaxation and electron spin resonance measurements led to the conclusion that eumelanin is a hybrid protonic-electronic conductor. Later on, Wuensche et al. quantified proton transport in eumelanin films, in a controlled humidity atmosphere, using proton 'transparent' electrodes ('protodes', made of palladium hydride)[134]. Reali et al., observing reversible electrical resistive switching in pellets of *dry* Sepia melanin, deduced that predominant electronic transport is possible in the biopigment[135], thus suggesting that the transport physics of dry eumelanin can be described by the amorphous semiconductor model.

It is important to highlight that *Sepia* melanin, as a *natural material*, has a complex chemical composition due to the presence of salts (e.g. cations such as Na^+ and Cu^{2+} and anions such as Cl^-, as detected by Neutron Activation Analysis)[136]. Such complex chemistry has to be taken into account when studying the electrical response of biosourced melanin. Open challenges in the field of melanin charge carrier transport physics are the polarity and nature of the charge carriers, the evolution of the ionic/electronic charge carrier ratio as a function of the chemical composition and material morphology/nanostructure and its impact on the density of charge carriers and mobility.

Magnetic properties and the role of radicals. Due to the presence of free radicals, melanins are paramagnetic (see Section 'Redox activity'). Free radical species can be studied using EPR and Muon Spin Resonance (muSR)[132,137,138]. Eumelanins are the most studied melanins using EPR, with the current understanding that there are at least two free radical species present: a 'Carbon Centred Radical' (CCR) and a 'Semiquinone Radical' (SQR)[139–141]. The magnetic response, especially EPR, can be modified by a wide array of parameters, including whether in solid state or suspension, pH, light, hydration, temperature and metal ion content[137,138].

The spectral response of the magnetic moments is consistent with chemical disorder, with the CCR likely due to the initial free radical polymerisation and the SQR due to the underlying quinone moieties manifesting equilibria such as a comproportionation reaction (Fig. 2d)[142]. These moments are intrinsically connected to the redox state, conductivity, presence of redox-active metals and thus implicated in eumelanin's radical scavenging and antioxidant properties[137].

However, the magnetic properties of eumelanin still hold mysteries. An outstanding question is whether more magnetic species are present beyond the CCR and SQR, noting that the CCR is still being investigated[141,143,144]. Recent structural work on eumelanin has suggested that the material may be a 'pancake bonded' system[145], where planar sheets participate in multi-site bonding due to the radicals (SQR) present. If true, this may result in weak ferromagnetism or anti-ferromagnetism.

The magnetic data obtained on melanins so far have been mostly acquired via continuous wave EPR. Thus, there is much scope for further elucidating the magnetic properties of eumelanin. Experiments for consideration should include: multifrequency EPR to resolve the different paramagnetic units' g tensors; pulsed EPR to explore dynamics (see ref. 146 as a rare example); EPR imaging to map out moment spatial distribution; electron-nuclear double resonance, electron spin echo envelope modulation and hyperfine-sublevel-correlation spectroscopy (HYSCORE) to probe electronic-nuclear magnetic interactions; double electron–electron resonance to probe electron–electron interactions; multi variable muSR (incl. temperature) to probe local magnetic ordering; magnetometry including superconducting quantum interference device (SQUID) measurements to quantify and detect macroscopic magnetic ordering as pioneered by the Gianneschi group[147,148].

Computational studies

The Eastbourne discussion highlighted how computational models can provide insights into eumelanin's structure and function. The thermodynamic stability[149], reactivity[150] and optoelectronic properties of 'bottom-up' oligomers have been studied with (Time Dependent) Density Functional Theory; aggregation properties of oligomers have been investigated using molecular dynamics simulations or stochastic models[151].

Given the large structural heterogeneity of melanin, combinatorial libraries of oligomers in various connectivity and oxidation states have proven useful for high-throughput studies. For instance, the computational study of libraries of DHI and DHICA oligomers of up to four units showed that planar structures tend to be more stable[152,153]. A study of a library of DHICA oligomers highlighted the key role of intra-molecular hydrogen bonds in creating strong dipole moments, localising excited states and determining the location of oxidised (quinone) units[154].

More recently, the thermodynamic stability of a comprehensive library of 830 DHI dimers[155] was investigated. The study found that oxidised structures are more stable, and polycyclic structures are favoured over linear ones. In addition, electrocyclisation of the linear dimers can yield polycyclic structures, which may be relevant for the formation of polycyclic, planar oligomers invoked in previous X-ray diffraction studies[69]. The calculated optical properties of these dimers reveal a range of bright optical absorption that spans the near UV to energies as low as 1.5 eV, ~800 nm. This supports the hypothesis that the characteristic broad electronic absorption of eumelanin may emerge from small chromophores.

Looking ahead, the generation of similar libraries for larger oligomers is challenged by combinatorial explosion. Machine learning (ML) approaches seem ideally suited to handle the large size of the expected data sets[120]. For instance, deep neural networks (DNN) have been shown to reproduce the ground and excited state energies of DHI dimers with errors of only 6 and 9%, respectively[156]. This suggests that properly trained DNN may predict the thermodynamic stability and optical properties of larger oligomers, paving the way for the use of ML models as a virtual screening tool.

Computational libraries of melanin oligomers should strive to be representative of the chemical heterogeneity of melanin; however, the paucity of molecular-level structural information has so far prevented constraining the models to realistic oligomer ensembles. This challenge may only be overcome by using high-resolution analytical data to constrain virtual libraries, and using computational data to interpret experiments, analogous to Omics approaches.

Melanin applications

Natural melanin is currently underrepresented in technologies and applications due to the characterisation challenges discussed above. With a few notable exceptions (Sections 'Dyes, coatings and paints' and 'Wound dressing and healing'), the discussion in Eastbourne mostly focused on applications based on natural melanin.

Dyes, coatings and paints

Melanin's exceptionally high refractive index and strong optical absorption[157] make it a promising optically active material for applications ranging from hair dyes[158,159], to advanced coatings and paints. Inspired by the vivid structural colours seen in birds[160,161], synthetic melanin nanoparticles have been engineered in a variety of applications. Xiao et al. reported synthetic melanin nanoparticle that self-assemble into ordered thin films; their coloration is based on thin film interference, and can be tailored by playing with the film thickness, humidity and evaporation rate[162]. Hu et al. have shown that micron-sized silica 'supraparticles' coated with melanin can be tailored to produce inks and paints across a broad spectrum of colours[163]. Thanks to their stability in both organic and aqueous solvents and improved mechanical properties, the silica-melanin formulation can be directly blended with painting and coating media. Synthetic melanin was shown to produce better absorption and colour purity compared to other polymeric counterparts, making it promising for optical coatings, sensors, and fade-resistant paints.

Wound dressing and healing

Both naturally occurring melanin and synthetic polydopamine (PDA) are highly appealing for biomedical and consumer applications, due to their radical scavenging activity[164] and excellent biocompatibility[165]. Protection

from reactive oxidative species is critical to successful wound healing[166]: an excess of radical species leads to molecular dysfunction, cellular damage, and inflammation; this prolonged oxidative stress and ultimately in impaired healing and development of chronic wounds[167].

One promising direction for PDA applications is the development of wound dressings based on PDA hydrogels[168]. They exhibit strong adhesive properties as well as the mechanical strength and compressive resilience needed for effective medical dressings. PDA-based hydrogels have been shown to support wound healing through their bacteriostatic and anti-inflammatory effects, while also providing a structural matrix that promotes cell adhesion, migration, and collagen deposition[168]. However, most of the current evidence is derived from small rodent animal models, and substantial clinical studies are still needed to confirm their efficacy and safety in human applications.

Biyashev et al. investigated the potential application of PDA nanoparticles to improve the healing of chemical injury wounds[169]. The study demonstrated that application of PDA protected the skin exposed to the toxic alkylating chemotherapy agent nitrogen mustard (known to cause cell death and skin blisters)[170–172]. Both natural and synthetic melanins offer a valuable platform for advancing both our understanding of skin biology and the development of next-generation skincare and therapeutic solutions.

Energy storage and sensing devices

The redox activity, conductivity and metal binding affinity of melanin are relevant for applications in electrochemical energy storage, organic electronics and sensors. If we exclude melanin-like materials and melanin-based composites, only a few proof-of-concept devices incorporate biosourced or biomimetic melanin—and solely rely on its intrinsic conductive properties. On the other hand, numerous studies have reported melanin-inspired or melanin hybrid materials for applications in energy storage[173], sensing[174–176] and optoelectronics[177].

Building on important results by Kim et al.[178] on melanin electrodes in aqueous sodium-ion energy storage devices, Gouda et al. demonstrated pseudo-supercapacitors (devices that combine electrical double-layer capacitance and surface-level redox processes to store charge) based on electrodes made up of Sepia melanin on treated carbon paper[179]. Al-Shamery et al. reported on eumelanin-based electrodes assembled into zinc coin cell devices employing a room temperature ionic liquid (RTIL) for high cycling stability[180]. Finally, Lee et al. demonstrated the use of natural melanin nanoparticles extracted from cuttlefish ink for conductive e-tattoos for biomedical applications[181].

Despite these recent advances, fundamental studies on the effect of the complex chemistry, environment and experimental conditions (atmosphere, temperature, illumination, interface with electrolytes and inter-electrode distance) on charge transfer and transport mechanisms are needed to rationally design melanin-based technologies and devices. When dealing with melanin films, the effect of the substrate surface on nucleation and growth (for bottom-up approaches) and supramolecular aggregation/complex chemistry (for top-down approaches) must also be considered.

Sustainable, biodegradable devices

There lies a significant interest in explicitly using biosourced melanin for sustainable and biodegradable applications, as eumelanin can be obtained in large quantities from renewable sources like fungi[182] and black soldier fly pupal exuviae[183]. The Royal Society meeting also included industrial melanin producers, demonstrating a growing interest in melanin valorisation.

Biodegradation of organic electronic materials and devices could help to mitigate the accumulation of electronic waste (e-waste)[184]. Composting, a waste management strategy used for organic waste, can bring rapid biodegradation in thermophilic conditions (50–60 °C), adequate water content (50–60 wt%), and a suitable population of microorganisms. During biodegradation, ecotoxicity tests must be performed to assess the effect of possible device components (e.g. metals) and biodegradation intermediates. Recent reports focused on the study of the biodegradation of Sepia melanin and Sepia melanin-based films printed on silver electrode-patterned paper. Di Mauro et al.[185] investigated the biodegradation of Sepia melanin under composting conditions following ASTM D5338 standard procedure (ISO 17088)[186]. They observed a mineralisation level of approximately 37% in 98 days and hypothesised that the (supra)molecular complexity of the biopigment inhibits complete enzymatic breakdown. The authors suggested that only the outer layers of Sepia melanin particles were accessible to enzymes. Conversely, the hygroscopic nature of melanin likely facilitates degradation, enabling enzymes to act more effectively. In a recent study, Camus et al.[187] explored printed films of Sepia melanin-shellac for compostable electronics. These conductive films printed on paper showed rapid biodegradation under composting conditions. Within 85 days, a level of mineralisation of 97% was reached, without any observable phytotoxic effects. Despite the small amount of Sepia melanin and shellac (5 wt.%), the mineralisation level was highly satisfactory. These results demonstrated the importance of having a biodegradable substrate to favour the biodegradability of devices.

Eom et al. introduced a novel approach using super-worms, i.e. larvae of the *Z. morios* beetle, to degrade melanin-polymer composites[188,189]. The incorporation of Sepia melanin into polyvinyl alcohol (PVA) enhanced biodegradation rates with respect to bare PVA when ingested by the larvae. This biologically driven method illustrates how nature-inspired solutions could address the structural challenges posed by melanin for biodegradation.

At the Royal Society meeting, we observed that the future of sustainable electronics lies not only in material sourcing and end-of-life management (e.g. biodegradation), but also in life-cycle assessment, to quantify the environmental impact of materials and processes. As research progresses, the eco-design of electronics must consider improving material sourcing and formulations to reduce the overall environmental impact of electronic devices. These considerations will facilitate the integration of melanin and, more broadly, sustainable electronic materials into industrial technologies.

Outlook

The Eastbourne meeting was the first international meeting entirely dedicated to melanin that combined expertise across disparate scientific disciplines, from chemistry, physics and materials science to evolutionary biology, palaeontology and medicine. Participants discussed advances in top-down and bottom-up synthesis and characterisation of melanin, highlighting its similarities to other carbon-rich materials (synthetic and natural organic matter) and the open controversies in the research community. The discussion on the evolution of melanin and its organelles highlighted how our knowledge of melanosome structure and melanogenesis in confined environments can aid in improving structural control in both biosourced and biomimetic/synthetic melanins.

Interest in melanin research has been rapidly growing: various proof-of-concept technologies have been demonstrated, and several small companies are now producing sustainable melanin at scale. However, manufacturing and commercialisation of melanin-based products and devices still requires a rigorous characterisation, towards an improved fundamental understanding of the chemistry and physics underpinning its unique properties.

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Competing interests

The authors declare no competing interests.

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