Supporting Information

for

Photoresponsive hydrogel networks using melanin nanoparticle photothermal sensitizers

By

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Figure S1. Temporal evolution of photothermal heating of MelNP dispersions with different concentrations ranging from 50 µg-mL⁻¹ to 20 mg-mL⁻¹. The predicted transient temperature profiles matched that of experimentally determined values at low concentrations of MelNP (< 5 mg-mL⁻¹). However, the temporal temperature profiles deviated significantly from experimental observations as the MelNP concentration was increased (See Text).

Detailed Calculations of Photo-Induced Heating of Melanin Nanoparticle Dispersions

MelNPs dispersions and MelNP-loaded hydrogels are prepared in scintillation vials to facilitate formation and optical thermal characterization. The heating rate of photo-induced aqueous melanin nanoparticle dispersions was determined by

\[ \sum m_i C_{p,i} \frac{dT}{dt} = Q_{in} - Q_{out} \quad \text{Eqn. S1} \]

In this equation, \( m_i \) and \( C_{p,i} \) represent the mass and heat capacity of component \( i \), \( T \) represents the temperature of the aqueous dispersion. The value of \( m_{H2O} \) and \( C_{p,H2O} \) were taken as 1 g per mL and 4.18 J-g⁻¹K⁻¹ respectively. The value of \( m_{MelNP} \) varies with MelNP concentration while 2.51 J-g⁻¹K⁻¹ was used as the value of \( C_{p,MelNP} \). The rate of energy supplied was calculated using Eqn 2.

\[ Q_{in}(z) = \frac{dI(z)}{dz} \quad \text{Eqn. S2} \]
The absorbed light intensity is calculated using the following relationship derived from the Beer-Lambert law.

\[ I = I_0 (1 - e^{-\beta z}) \quad \text{Eqn. S3} \]

\( I_0 \) was measured to be 10.8 mW-m\(^{-2}\). The value of \( \beta \) was estimated using the following input parameters for Mie scattering (reference 34 in main text). Briefly, the refractive index mismatch ratio \((n_{\text{MelNP}}/n_{\text{water}})\) and the size parameter \((x = 2\pi D_{\text{MelNP}}/(\lambda n_{\text{water}}))\) were calculated. The indices of refraction of melanin and water are given by \( n_{\text{MelNP}} = 1.3 \) and \( n_{\text{water}} = 1.33 \), respectively. The value \( N_{\text{MelNP}} \) represents the number density of MelNP nanoparticles in solution assuming a spherical particle of diameter \( D_{\text{MelNP}} = 2R_g = 200 \) nm. This calculation uses a melanin mass density of 1.68 g-cm\(^{-3}\) (reference 28 in main text). We used an algorithm to calculate the efficiency of scattering \( Q_s \) (reference 40 in the main text). Briefly, the algorithm was based on the following equation:

\[ Q_s = \frac{2}{x^2} \sum_{n=1}^{N} (2n+1)(|a_n|^2 + |b_n|^2) \quad \text{Eqn. S4} \]

where the complex Mie coefficients \( a_n \) and \( b_n \) were functions depending on \( x \) and the complex refractive index\(^3\). The output values of \( \beta (Q_s S A_{\text{MelNP}} N_{\text{MelNP}}) \) are summarized in Table S1.

<table>
<thead>
<tr>
<th>MelINP conc, ( c_{\text{MelNP}} ) (mg-mL(^{-1}))</th>
<th>0.05</th>
<th>0.1</th>
<th>0.2</th>
<th>1</th>
<th>5</th>
<th>10</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scattering coefficient ( \beta \times 10^{-2} ) (cm(^{-1}))</td>
<td>0.1090</td>
<td>0.1109</td>
<td>0.1330</td>
<td>0.160</td>
<td>0.747</td>
<td>1.254</td>
<td>2.259</td>
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</table>

Heat loss was dominated by radial thermal conduction through the walls of the glass vials. The rate of heat loss \( Q_{\text{out}} \) is calculated using Eqn 4:
\[ Q_{\text{out}} = -k_{\text{SiO}_2} S \frac{dT}{dr_{\text{shell}}} \]  

Eqn. 4

In this expression, \( k_{\text{SiO}_2} \) represents the heat transfer coefficient of silicon oxide (1 W-m\(^{-1}\)-K\(^{-1}\))^2, \( S \) is the surface area of conduction and \( r_{\text{shell}} \) is the coordinate within the silicon oxide shell between the inner (\( R_{\text{in}} \)) and outer radii (\( R_{\text{out}} \)) of the conduction path where \( |R_{\text{out}} - R_{\text{in}}| \ll R_{\text{in}} \). The symbol \( k_{\text{SiO}_2} \) represents the heat transfer coefficient of silicon oxide (1 W-m\(^{-1}\)-K\(^{-1}\)). The inner (\( R_{\text{in}} \)) and outer (\( R_{\text{out}} \)) radii was measured to be 1.59 cm and outer radii (\( R_{\text{out}} \)) was 1.68 cm.
Figure S2. Phase transition behavior of hydrogel formed from 200 mg-mL\(^{-1}\) PLGA-PEG-PLGA concentrations. Loading MelNP expands the gel transition of the hydrogel by accelerating sol-gel transition and retarding precipitation (See Text).
Figure S3. Phase transition behavior of hydrogel formed from different PLGA-PEG-PLGA concentrations: a) 100 mg-mL$^{-1}$, b) 150 mg-mL$^{-1}$, and c) 250 mg-mL$^{-1}$ with and without 1 mg-mL$^{-1}$ MelNP. Loading MelNP expands the gel transition of the hydrogel by accelerating sol-gel transition and retarding precipitation (See Text).
Figure S4. Hydrogel formed from 200 mg-mL\(^{-1}\) solution of PLGA-PEG-PLGA doped with 1mg-mL\(^{-1}\) MelNP was exposed to UV light. No change in \(G'\) was observed over irradiation time, suggesting that the decrease in \(G'\) of PLGA-PEGPLGA hydrogel with embedded MelNP (Fig. 7) resulted from the photothermal response of the MelNP. A slight increase of \(G''\) was observed possibly due to dehydration of the hydrogel during UV irradiation time.
Figure S5. Size distribution of MelNP at concentration 1 mg-mL$^{-1}$ was measured by dynamic light scattering.
Figure S6. Size distribution of pristine PLGA-PEG-PLGA micelles was measured by dynamic light scattering at 25, 37, and 45 °C.
Figure S7. Amplitude sweep of hydrogel PLGA-PEG-PLGA doped with 1mg-mL⁻¹ MelNP at $\omega = 5$rad/s shows that the parameter chosen (0.5% strain) is in the linear viscoelastic regime.
Figure S8. Photothermal response of hydrogel formed from 200 mg-mL$^{-1}$ PLGA-PEG-PLGA to UV irradiation shows an increase of 5.4 ± 0.6 °C. This temperature increase is significantly smaller compared to the increase of 20.4 ± 0.1 °C that is achievable with aqueous dispersions of 1 mg-mL$^{-1}$ MelNP (Fig.3).
Figure S9. Photographic images of hydrogel formed from 200 mg-mL$^{-1}$ PLGA-PEG-PLGA doped with 1 mg-mL$^{-1}$ MelNP undergoing phase transitions from SOL to GEL to PRECIPITATE after UV irradiation for 30 minutes.
Table S2. The total free energy of adsorption of PLGA-PEG-PLGA to MelNP ($\Delta G_{\text{ads,vol}}$) was calculated and compared to the competing process of gelation ($\Delta G_{\text{gel}}$). This calculation is consistent with the trends in gelation versus MelNP concentration (See Text).

<table>
<thead>
<tr>
<th>MelNP Concentration $c_{\text{MelNP}}$ (mg-mL$^{-1}$)</th>
<th>$\Delta G_{\text{ads,vol}}$ (J-mL$^{-1}$)$^a$</th>
<th>$\Delta G_{\text{gel}}$ (J-mL$^{-1}$)$^b$</th>
<th>Gel formation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05</td>
<td>-0.05</td>
<td>-6.1</td>
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<tr>
<td>0.1</td>
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<td>&quot;</td>
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<tr>
<td>20</td>
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<td>&quot;</td>
<td>No</td>
</tr>
</tbody>
</table>

$^a$Calculated from Eqns. 5 and 6 of main text.

$^b$Constant value for all compositions. Taken from reference 45 of main text.

Additional References