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Dual-Responsive Nanoparticles that Aggregate under the Simultaneous Action of Light and CO\textsubscript{2}

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Metallic nanoparticles co-functionalised with monolayers of UV- and CO\textsubscript{2}-sensitive ligands were prepared and shown to respond to these two types of stimuli reversibly and in an orthogonal fashion. The composition of the coating could be tailored to yield nanoparticles capable of aggregating exclusively when both UV and CO\textsubscript{2} were applied at the same time, analogously to the behaviour of an AND logic gate.

Stimuli-responsive nanomaterials\textsuperscript{1} that self-assemble in a reversible fashion are important for their emerging applications in diverse fields, such as switchable catalysis\textsuperscript{,2-3} water purification\textsuperscript{4}, detection of analytes\textsuperscript{,5} and time-sensitive information storage\textsuperscript{.6} Accordingly, a variety of nanoparticles (NPs) have been engineered to aggregate in response to different external stimuli, such as a magnetic field\textsuperscript{,7} pH\textsuperscript{,8,9} or chemical fuel\textsuperscript{.10} For example, dynamic aggregation of metallic NPs was accomplished by reversibly photoswitching the electronic states and geometries of surface-bound chromophores\textsuperscript{,11-14} New applications could arise, however, for NPs that respond to two (or more) different external stimuli at once, such as the recently reported dual-responsive NPs that aggregate when either a magnetic field or light is applied\textsuperscript{.15-18} Whereas such dual-responsiveness is, in principle, relatively easy to "encode" in the NPs, it is more challenging to design systems capable of aggregating only when two types of external stimuli are applied at the same time\textsuperscript{.19-20} Here, we describe the first system exhibiting such behaviour with light and carbon dioxide as the two "inputs".

Carbon dioxide is a biocompatible, naturally abundant gas that has several advantages over other chemical stimuli: \textit{i}) facile reactivity with various nucleophilic Lewis base functional groups such as amines, NHCs (N-heterocyclic carbenes), or guanidines, \textit{ii}) easy removal from the above complexed by mild heating, sonication, or purging with an inert gas, \textit{iii}) no by-product formation through the reversible complex formation, and \textit{iv}) potential applicability to reversible CO\textsubscript{2} capture and/or transformations\textsuperscript{.21-24} In addition, nanomaterials that aggregate reversibly in the presence of CO\textsubscript{2} are potentially important as possible anti-cancer therapeutics (taking advantage of the increased production of CO\textsubscript{2} in cancer cells)\textsuperscript{,25-26} Although many CO\textsubscript{2}-sensitive materials\textsuperscript{,27} in particular, organic polymers\textsuperscript{,28-29} have been reported, the application of amine-functionalised metallic NPs as CO\textsubscript{2}-responsive materials remains unknown. Here, we presumed that control of the NP surface polarity by using fine-tuned amounts of photo- and CO\textsubscript{2}-sensitive ligands could induce selective and reversible aggregation of NPs with two orthogonal stimuli (Figure 1).

It is well established that mixtures of \textit{ω}-functionalised long-chain alkanethiols can form mixed self-assembled monolayers (mSAMs) on the surfaces of metallic NPs\textsuperscript{.30} (here, we focused on gold NPs). We commenced our study with AuNPs functionalised with mSAMs comprising an azobenzene-terminated thiol (AzoSH) and a "background" ligand, 1-dodecanethiol (C\textsubscript{12}SH) (Figure 2a). As the UV-Vis spectra in Figure 2b show, NPs decorated with critical (>50\%) amounts of AzoSH aggregate in toluene upon exposure to long-wave (\(\lambda = 365\) nm) UV light\textsuperscript{,31} whereas they exhibited no detectable response to CO\textsubscript{2} (confirmed by dynamical light scattering (DLS) measurements; see ESI\textsuperscript{1}, Figure S2 in Section 5). Furthermore, we observed that the \textit{trans}-to-\textit{cis} photoisomerisation of AzoSH did not affect the affinity of these NPs towards CO\textsubscript{2} (Figure S2). Therefore, we concluded that those AuNPs bearing only the AzoSH and C\textsubscript{12}SH ligands are inert towards the CO\textsubscript{2} stimulus under these conditions.

The lack of general knowledge on the construction of CO\textsubscript{2}-sensitive metal-nanoparticle surfaces encouraged us to investigate the synthesis and application of thiol-terminated amine ligands (Figure 1b)\textsuperscript{32} Based on previous literature reports\textsuperscript{,33-36} we presumed that ethylenediamine derivatives are capable of CO\textsubscript{2} complexation under low-pressure conditions. To verify the effect of CO\textsubscript{2} binding on the solubility in toluene, we synthesized and studied the behaviour of a model compound, N-decylethlenediamine. As detailed in the SI (Section 3), this diamine was readily soluble in toluene; however, rapid precipitation commenced upon bubbling CO\textsubscript{2} through the solution (Fig. S1). The process was reversible: the addition of an inert gas (e.g. N\textsubscript{2}) caused the precipitate to redisolve. Encouraged

![Figure 1](image-url)
by these results, we then proceeded to synthesise AuNPs decorated with the diamine moieties. Although diamine-functionali- 
cated NPs were previously prepared by reacting 11- 
bromoundecane-1-thiol (2)-decorated NPs with 1,2- 
ethylenediamine, we began our investigation by preparing a well- 
defined thiol bearing the diamine moiety. As shown in Scheme 1, 
the synthesis of diamine 3 was straightforward, starting with a 
known material.14-16

Scheme 1. Synthesis of diamine ligand 3.

With the diamine-functionali- 
te thiolate ligand 3 in hand, we 
prepared a family of dual stimuli-responsive AuNPs by varying 
the ratio of the two responsive ligands (AzoSH and diamine 3) 
and the background ligand 1-dodecanethiol (C12SH), as shown in 
Figure 3. Although 3 could potentially bind to AuNPs via both 
the mercapto and the amine functionalities, the latter scenario is 
unlikely given the ca. two-orders-of-magnitude higher affinity of 
Au to thiols as compared to amines.17 In addition, binding to Au 
via the amine functionalities would cause NP crosslinking and 
irreversible aggregation, which we did not observe.18

Owing to the high polarity and low toluene solubility of the diamine 
ligand 3, the ligand exchange reaction was conducted under diluted 
(ca. 10 times) conditions, compared with typical ligand exchange 
reaction conditions.19 Moreover, 3 was always used after drying 
under vacuum at 40 °C to ensure that it was not complexed with 
CO2. The functionalised AuNPs were precipitated with methanol 
(1:1 v/v) in the presence of didodecylmethylammonium bromide 
(0.5 mg per 0.716 mg of Au), washed extensively with methanol 
to remove any unbound molecules, dried under vacuum and kept 
in an inert atmosphere prior to use. A good indication of the pre 
sence of 3 on the functionalised AuNPs is their good solubility in polar 
solvents (e.g., ethanol, methanol and even water), which confirms 
a successful ligand-exchange reaction (for a comparison, AuNP- 
AzoSH are only soluble in non-polar solvents such as toluene, 
chloroform, or dichloromethane). The functionalisation procedure 
did not affect the size or size distribution of the NPs, whose monodispersity 
was confirmed by transmission electron microscopy (Figure 5a).

Fine-tuning of the ratio of the three ligands was critical for 
obtaining NPs exhibiting the behaviour shown in Fig. 1c (in this 
context, it is worth mentioning that the previously adapted 
on nanoparticle reaction between ethylenediamine and 2-functionali-
AuNPs would hardly be applicable. We found that when the molar percentage of 3 on the NPs exceeded 25%, the particles were insoluble in toluene due to their high surface polarity. These aggregated NPs could not be redissolved using visible light, sonication, or by purging with N₂ (to remove any possibly complexed CO₂). Therefore, the amount of the diamine 3 was fixed at 25% throughout the optimisation of the mSAM composition. Having screened the ratio of the remaining two ligands (AzoSH and C₁₂SH) from 1:2 to 2:1, we found that NPs containing 33-35 mol% of AzoSH within the mSAM exhibited the behaviour shown in Fig. 1c. According to DLS, these NPs had hydrodynamic diameters of 7-10 nm in toluene, and did not aggregate with either only UV irradiation or CO₂ treatment (bubbling into the solution) (red and blue bars, respectively, in Figure 3). Only when both stimuli were applied at once (4 min of UV irradiation during CO₂ bubbling), however, did the NPs rapidly assemble into aggregates of 800-1000 nm in size, as shown by DLS (green bars in Figure 3). The presence of aggregated NPs was also evident from TEM and spectroscopic analysis (Figure 5b, c). Interestingly, these aggregates were stable in a closed vial placed in the dark for more than 30 minutes.

![Figure 5](image-url)

**Figure 5.** (A) TEM images of AuNPs before aggregation. (B) The same NPs after applying two stimuli (CO₂ and UV) at once. (C) UV spectra of AuNPs with only one stimulus (red and green) and both stimuli at once (cyan). The scale bars in TEM images are 50 nm.

Further demonstration of the AND gate-like behaviour was provided by removing one of the two stimuli. For example, when a solution of aggregated NPs was sonicated, facile disaggregation was observed even under constant UV irradiation (yellow bars in Fig. 4c; ca. 10 nm). The resulting NPs did not respond to only CO₂ or UV, but they could again be quickly aggregated by applying UV and CO₂ simultaneously (second-cycle green bars in Figure 4 and the TEM image in Figure 5b). Interestingly, our NPs also assembled as a result of CO₂ bubbling (4 min), followed by exposure to UV light, or via the opposite sequence, whereby UV-irradiated NPs were treated with CO₂ in the dark: these results indicate that both i) cis-azobenzene and ii) the CO₂-diamine complex is relatively stable, i) in the dark, and ii) unless other stimulants (such as sonication, heating or inert gas bubbling) are applied.

Thus assembled AuNPs readily disaggregated under ambient light (5-6 minutes) or upon exposure to visible light (fluorescent bulb, <30 seconds), and consequently, additional assembly-disassembly cycles could be performed. Overall, we concluded that this study represents the first example of CO₂- and light-responsive nanoparticles, whose behaviour constitutes an AND logic gate. Noteworthy, NPs having higher surface concentrations of AzoSH did respond to UV light by assembling into aggregates, which could aggregate further upon the delivery of CO₂ (SI, Figure S6C). In other words, only upon pre-exposure to UV light were these specific NPs responsive to CO₂.

**Conclusions**

We prepared gold nanoparticles co-functionalised with azobenzene- and diamine-based ligands, which rendered the particles responsive to UV irradiation and CO₂, respectively. Exposure to UV and CO₂ each led to a stepwise increase in the nanoparticle surface polarity, triggering aggregation in a non-polar medium (toluene). The composition of the mixed monolayer of ligands could be tuned in order to afford NPs capable of aggregating only when both types of stimuli are applied at once. Both of these stimuli could easily be turned off / removed without the generation of any by-products / chemical waste, after which the assembly-disassembly cycles could be repeated. The aggregates only exist when both light and CO₂ are delivered simultaneously. An important future direction concerning these and other man-made dynamically aggregating materials is to study / engineer their emergent behaviours under non-equilibrium conditions.

**Notes and references**

Under our experimental conditions, transformation of the carbamate into a cyclic urea is highly unlikely as it typically requires high CO$_2$ pressures, elevated temperatures, and/or the presence of a catalyst (e.g. Ref. 38, 39).

This conclusion is supported by an experiment in which we incubated AuNPs co-functionalized by 3 and C$_{12}$SH under oxygen for an extended period of time. Under the oxidative conditions, the presence of free SH groups on the outer surfaces of NPs would likely cause crosslinking due to disulfide bridge formation. No such crosslinking was observed by DLS or UV-Vis spectroscopy.

In addition to the increasing NP surface polarity in the nonpolar medium, attractive forces between the NPs could originate from direct interactions (e.g. due to dipole-dipole interactions of the cis-azobenzene dipoles).