**Electro-click construction of Hybrid Nanocapsule Films with Triggered Delivery Properties**

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Figure S-1: Size characterization of the inorganic nanoparticles and of hybridosomes. a) TEM micrograph of a single Hybridosome corresponding to the first slice of the S-1 video. b) Size distribution of a Hybridosome in aqueous dispersion, measured by Nanoparticles Tracker Analysis (NTA), which allows the mean-size and the concentration of Hybridosomes suspensions to be calculated. NTA tracks individual trajectories, allowing the calculation of the diffusion coefficient and thus of the hydrodynamic diameter of each particle. NTA was carried out with a Nanosight LM10 device system equipped with a 40 mW laser working at λ = 638 nm. Video sequences were recorded via a CCD camera operating at 30 frames per second and evaluated via the NANOSIGHT NTA 2.0 Analytical Software Suite. The hybridosomes suspensions at [Fe] ~50µg/mL are washed two times after magnetic separation and diluted 100 times before NTA analysis. c) Characteristic TEM picture and size histogram distribution of pristine iron oxide nanoparticles.
Video S-1: TEM tomography of a single Hybridosome®.

Reconstructed video obtained from 76 tomography-slices measured from –60° to +15° with a 1° increment.

https://mycore.core-cloud.net/public.php?service=files&t=10205a71e3d5fd4d80dc4370f2b0812c

Polymer grafting degrees.

- Estimation of the grafting degree of PAA-C≡CH by 1H NMR.

We arbitrarily fixed the integration value of the alkyne CCH signal of PEG (2.83 ppm) at 1. From a comparison of the integration values of signals between 3.72-3.16 ppm (NHCH2, CH2NH, CH2OCH2 of PEG) and those between 2.52-1.37 ppm (CH2CHCO of PAA and CH2CH2CH2CCH of PEG), the effective degree of modification was estimated to be 6%.

1H NMR assignment in ppm (500 MHz, 10% D2O): 8.07 (b, CONHCH2), 4.16 (s, OCH2CCH), 3.67 (bm, CONHCH2CH2O), 3.62 (bs, OCH2CH2O), 3.52 (bm, CONHCH2CH2O), 2.83 (s, OCH2CH2CH2), 2.29 (bs, CH(COOH)CH2), 1.82 (b, CHCH2), 1.64 (b, CH(COOH)CH2), 1.53 (b, CH3CH).

Scheme S-1: Synthesis of PAA-C≡CH.

- Estimation of the grafting degree of PEI-C≡CH by 1H NMR.

We arbitrarily fixed the integration value of the signals resonating between 1.66 ppm and 0.97 ppm at 12 (according to the corresponding number of protons contained in the repetition unit of the polymer). From a comparison of the integration values of signals between 3.1 and 2.3 ppm (NH2CH2N of the grafted 10-undecyanoic acid), the effective degree of modification was estimated to be 12%.

1H NMR assignment in ppm (500 MHz, 10% D2O): 3.35 (bs, NH2CH2), 3.18 (s, CONHCH2CH2), 2.92/2.76/2.63/2.55 (b, NCH2CH2N), 2.07 (bs, NHCOCH2CH2), 1.41/1.28/1.18 (b, CH2CH2CH2).

Scheme S-2: Synthesis of PEI-C≡CH.
Figure S-2: ATR-FTIR Spectroscopy of functionalized polymers. a) ATR-FTIR spectra of PAA (black line) and PAA-C≡CH (red line). b) Typical ATR-FTIR spectra of PEI (black line) and PEI-C≡CH (red line) with characteristic bands of Amide 1540cm$^{-1}$ and 1640 cm$^{-1}$, and characteristic peak of the bending vibration C-H from the undecynoic acid grafted pendant chain.

Figure S-3: Buildup of the film. Typical SEM micrographs of the deposited material on FTO (a) in absence of CuSO$_4$, (b) in absence of N$_3$-PEG-N$_3$ linker, and (c) in absence of any applied potential. (d) Electro-clicked nanocapsule film obtained by using typical conditions (-0.2 V to 0.6 V vs Ag/AgCl, 50 mV/s in the presence of 4.5 × 10$^9$ Hybridosomes/mL 0.1 mg/mL N$_3$-PEG-N$_3$ and 0.6 mM CuSO$_4$ at pH 3.5).
Figure S-4: Click reaction occurrence. (a) ATR-FTIR spectra of PEI-C≡CH (black line), PAA-C≡CH (red line), N_3-PEG-N_3 linker (blue line) and of the film (green line) constructed under typical conditions (-0.2 V to 0.6 V vs Ag/AgCl, 50 mV/s in the presence of 4.5 × 10^9 Hybridosomes/mL, 0.1 mg/mL N_3-PEG-N_3 and 0.6 mM CuSO_4 at pH 3.5). (b) Corresponding peak assignments.
Figure S-5: Evolution of the intensity-potential diagram during the film construction. (a) Voltamogram corresponding to the buildup of a Hybridosome electroclicked film during 800 CV cycles under typical conditions (-0.2 V to 0.6 V vs Ag/AgCl, 50 mV/s in the presence of $4.5 \times 10^9$ Hybridosomes/mL, 0.1 mg/mL $N_3$-PEG-$N_3$ and 0.6 mM CuSO$_4$ at pH 3.5); (b) Evolution of the maximum intensity of the copper oxidation peak, measured at 90 mV, in function of the CV cycle number.

<table>
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<th>CV number</th>
<th>Average surface coverage by the film(%)</th>
<th>Average thickness of the covered area (nm)</th>
<th>Roughness (RMS) of covered areas (nm)</th>
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<tr>
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<td>0</td>
<td>0</td>
<td>33</td>
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<tr>
<td>25</td>
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<tr>
<td>800</td>
<td>92</td>
<td>845</td>
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Table S-1: Evolution of the film roughnesses during the electroclick deposition process. Roughnesses were obtained by calculating the root mean square (RMS) of the AFM cross-section data, in contact mode and in the dried state, corresponding to the area covered by the film, at 25, 100 and 800 CV cycles. The initial roughness of the FTO electrode (0 cycles) was calculated by calculating the RMS of the full AFM height image (20x20 μm$^2$) of bare FTO.
Figure S-6: Film growth, thickness evolution. AFM images and corresponding thickness profiles of (a) adsorbed Hybridosomes and films obtained under typical conditions after (b) 25, (c) 100 and (d) 800 CV cycles.
Figure S-7: Chemical and structural stability of Hybridosomes® along the film construction process. a) Voltamogram of 50 cycles from -1V to 1V (vs Ag/AgCl) at pH 3.5 of a Hybridosome dispersion. (b) Size distribution of Hybridosomes, calculated from low-magnification SEM micrographs with ImageJ, of adsorbed nanocapsules on a STEM grid (black bars) and after inclusion of the nanocapsules in the electro-clicked film (red bars).

Figure S-8: Chemical composition of films constructed with IONPs based Hybridosomes®. a) SEM micrograph of a film assembled in typical electro-click conditions after 800 CV cycles. (b) Corresponding EDX analysis of the film. c) Element analysis of the corresponding zone of the film.
Loading efficiency of hybridosomes

The BODIPY dye absorbs both in solution and in the solid state. It is mostly water insoluble, so that we expect the BODIPY to be under the form of nanoprecipitated particles, both in the supernatant and in the core of the hybridosomes. Fig S-10a shows the absorbance spectra of the BODIPY-containing hybridosomes after washing twice (blue line), together with the supernatants of the first (black line) and second washes (red line). Importantly, the second supernatant is completely clear of bodipy, indicating that the encapsulated dye does not leak spontaneously. Note that the optical signal due to absorbance and scattering of the IONPs hybridosomes adds a significant background to the signal. However, after correction of the baselines, a rough comparison of the peaks area between the first wash supernatant and the bodipy-loaded hybridosomes, suggest that 73 % the bodipy was encapsulated.
Figure S-11: Surface area of fluorescence emission bands (a) calculated by integration of the corresponding peaks between 510 nm and 700 nm. (b) Linear regression ($y = 1783.x + 2159; R^2=0.99$) of the peak areas in function of the “loading/empty” nanocapsules ratio in the building solution.

<table>
<thead>
<tr>
<th>L/E ratio (%)</th>
<th>Peak area (a.u.)</th>
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<tr>
<td>10</td>
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<tr>
<td>50</td>
<td>82 000</td>
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<tr>
<td>90</td>
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Figure S-12: pH sensitivity of functionalized “clickable” Hybridosomes® dispersions. Multiscale SEM analysis of Hybridosomes dispersions after 15 min of incubation with HCl solutions of pH 4 (a,b) pH 3.5 (c,d), pH 3 (e,f) and pH 1 (g,h).
Figure S-13: pH sensitivity of electro-clicked Hybridosome®-based films. SEM micrographs of electro-clicked Hybridosome films obtained after 800 CV cycles and incubated 15 min in HCl solutions of pH 1 (a), pH 2.5 (b), pH 3 (c) and pH 3.5 (d).
Figure S-14: pH-triggered release abilities of electro-clicked Hybridosomes®-based films. SEM micrographs (a, b) and fluorescence spectra ($\lambda_{\text{exc}}$ at 480 nm) in the dry state (c, d) of bodipy-loaded Hybridosome films constructed on ITO (black line) and of the corresponding supernatant (red line) before (a,c) and after (b,d) application contact with a 0.1M HCl solution for 15min.
Figure S-15: Cargo release under electrochemical stimulus. SEM micrographs with higher magnification before (a) and after (b) applying +1 V potential vs Ag/AgCl for 15 min in a 0.1 M NaCl solution.