Supporting Information

"Controlling the nano-bio interface to build collagen/silica selfassembled networks"

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Characterization of silica particles by X-ray photoelectron spectroscopy (XPS)

Figure S1. XPS of non-functionalized Stöber particles: (a) full spectrum, and enlargement of the binding energy regions characteristic of (b) oxygen and (c) silicon.



Figure S2. XPS of thiol-functionalized Stöber particles: (a) full spectrum, and enlargement of the binding energy regions characteristic of (b) oxygen, (c) carbon, (d) sulfur, and (e) silicon. The peak observed at 163-164 eV is characteristic of thiol groups.



Figure S3. XPS of sulfonate-functionalized Stöber particles: (a) full spectrum, and enlargement of the binding energy regions characteristic of (b) oxygen, (c) carbon, (d) sulfur, and (e) silicon. The peak observed at 169 eV confirms the oxidation of thiol groups.

Investigation of the 3D networking of the hybrids

This part presents additional investigations of the 3D networking of the hybrids, in particular nucleation studies of collagen fibrils with various nucleation conditions. These experiments are schematically described below (Scheme S1) and concern: (I) the initial state of the building block used to induce fibrillogenesis (in terms of concentration and pH), and (II) a deeper investigation of the effect of a change in collagen/nanoparticle ratio (R).



I. Concentration / pH of the starting building block

II. Varying collagen/particle ratio (R)



Scheme S1. Representation of the different set-up investigated to understand the 3D networking process in collagen-silica networks.

I. Concentration / pH of the starting building-block.

This part aims at understanding the importance of collagen conformation at the particle surface, before triggering fibrillogenesis. Experiments showed that extended fibrils were observed at a collagen ratio R = 3400 but not for R = 240 - 340. The question arises about the possibility to build networks from the brush-like particles (R = 240 - 340) by increasing R to 3400 in a second step. To focus on the starting conformation of collagen at the particle surface, two set up were investigated:

- I(a). Addition of collagen to brush-like particles in acidic medium (pH 2.5, $R_{final} = 3400$) before increasing pH to induce fibrillogenesis (final pH~ 6.5). In this case, extended networks were observed.
- I(b). In a second experiment, collagen addition ($R_{final} = 3400$) was performed after increasing the pH to 6.5 (final pH~6.5). In other words, collagen was added to pregrown fibrils nuclei. Again, extended fibrils were observed.

II. Varying collagen / particle ratio (*R*).

Finally, various collagen / particles ratios were investigated in between the two values described in the manuscript (R = 340 no networking; R = 3400 3D networking). TEM observations of the different samples show that in all cases, collagen fibrils could be observed, exhibiting increasing length and density with R (Figure S1).



Figure S4. TEM of collagen:NP-SiSO₃. (a) R = 750, (b) 1250, (c) 2750 ([SiO₂] = 22.5.10⁻³ M, pH 6.5).

All together, these data show that the surface chemistry of the particle is a key point to confine collagen and promote the growth of fibrils and 3D networking (NP-Si *vs* NP-SiSO₃). However, the conformation of collagen at the particle surface does not seem to be critical for 3D networking (soluble monomer or assembled nuclei). Indeed, whenever collagen is initially confined at the particle surface, it can further self-assemble from the particle, provided that an excess of collagen is present (*i.e.* final R > 240).