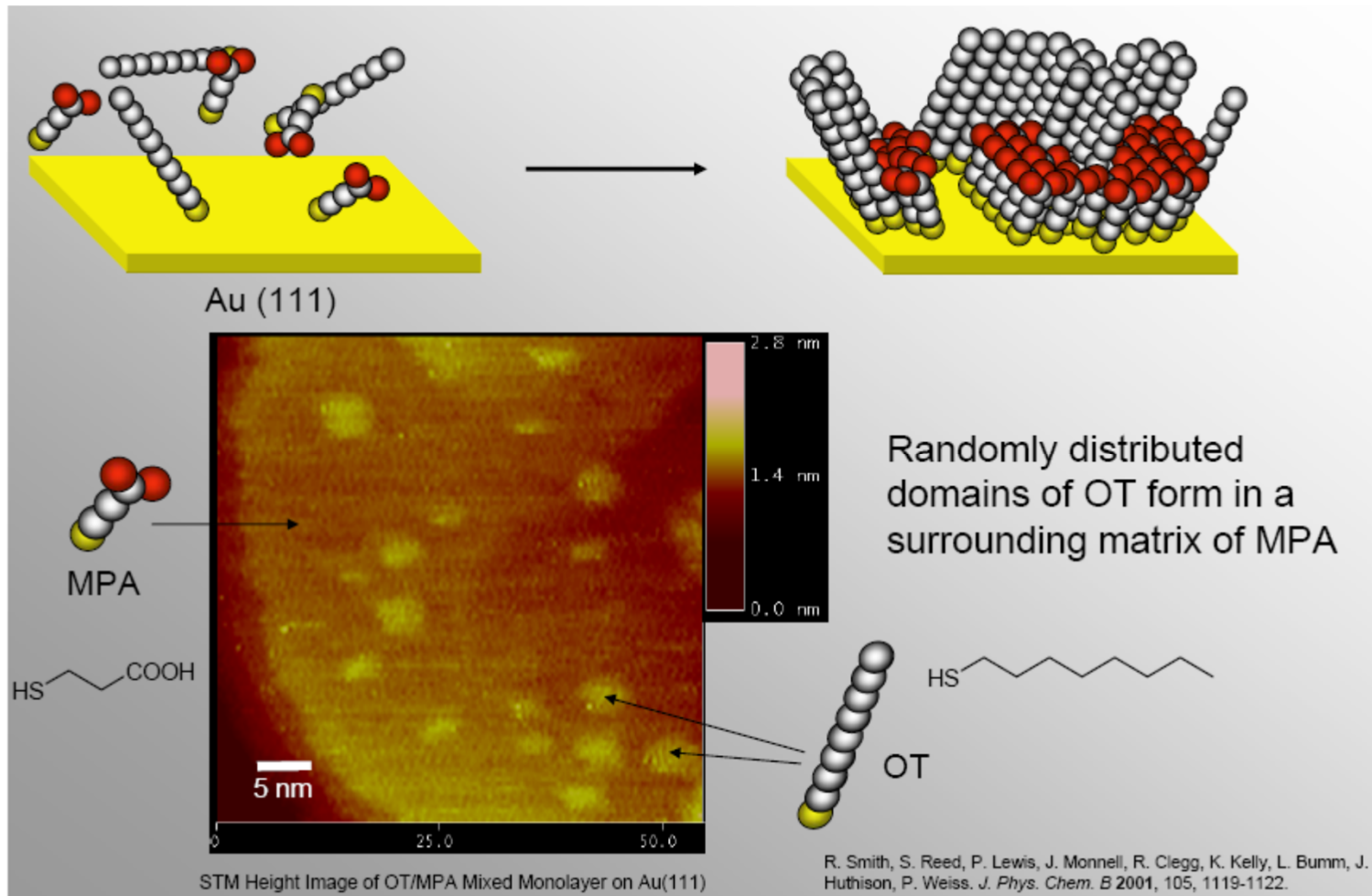


Mixed 3-D SAM

Mixed Self-Assembled Monolayers



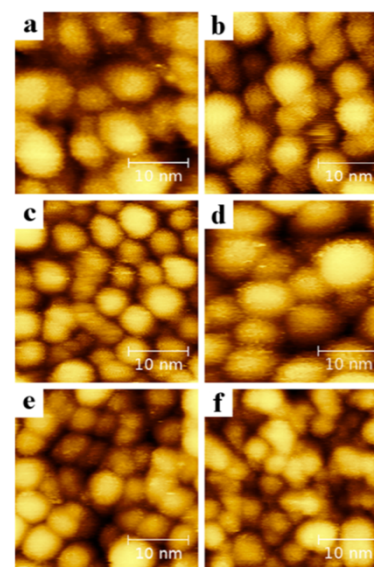
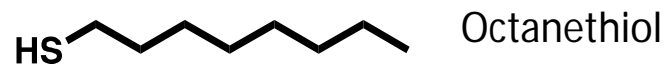
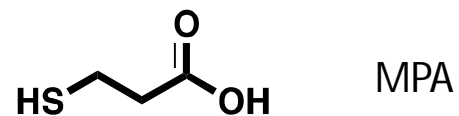
Ordered Domains on NPs

Quantitative Analysis of Scanning Tunneling Microscopy Images of Mixed-Ligand-Functionalized Nanoparticles

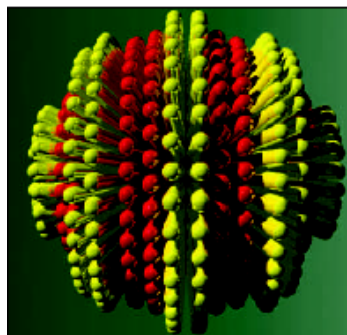
Fabio Biscarini,^{*,†} Quy Khac Ong,[‡] Cristiano Albonetti,[§] Fabiola Liscio,^{||} Maria Longobardi,[⊥]
Kunal S. Mali,[#] Artur Ciesielski,[○] Javier Reguera,[‡] Christoph Renner,[⊥] Steven De Feyter,[#] Paolo Samori,[○]
and Francesco Stellacci[‡]

Langmuir 2013, 29, 13723–13734

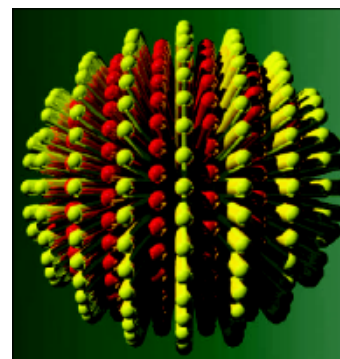
topographical power spectral density (PSD)



organization of mixed-monolayers



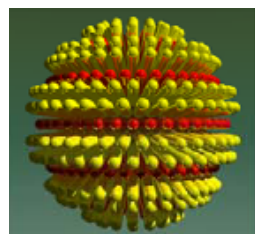
OT/MPA 2:1



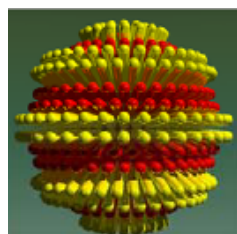
Decanethiol/MPA 2:1

d 3.7 nm

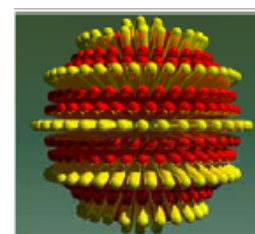
MPA/MPA+OT



5:1 3:1



2:1 1:1



1:2 1:3

Jackson, A. M et al Nat. Mat., **2004**, 3, 330; Jackson, A. M. et al J. Am. Chem. Soc., **2006**, 128, 11135;

organization of mixed-monolayers

methods of characterization

- ◆ STM Scanning tunneling microscopy
- ◆ AFM
- ◆ TEM (CryoTEM)

- ❖ SANS Small angle neutron scattering
- ❖ MS mass spectrometry
- ❖ NMR Nuclear magnetic resonance
- ❖ FT-IR infrared spectroscopy
- ❖ ESR electron spin resonance

- MD-DPD Molecular dynamics-dissipative particle dynamics
- Monte Carlo simulations

- ✓ activity
- ✓ interaction with environment – solubility, interactions with cells (membranes), etc.

microscopy

spectroscopy

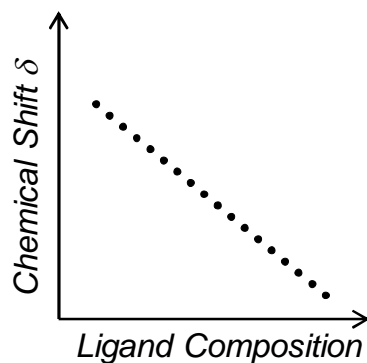
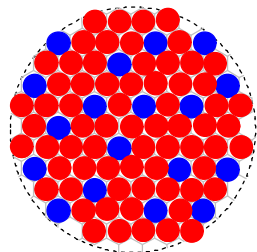
simulations

Predicted NMR patterns for nanoparticles coated with a binary mixture of ligands

Chemical shift behaviour

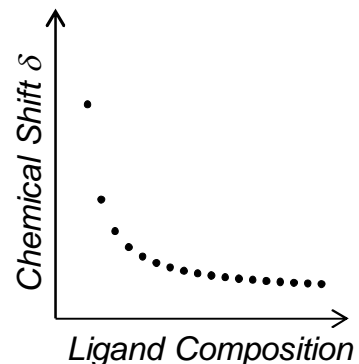
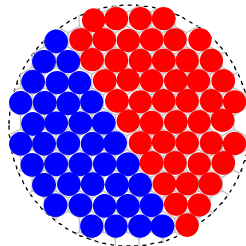
Random

$$\delta = \delta_B x_A + \delta_I (1 - x_A)$$



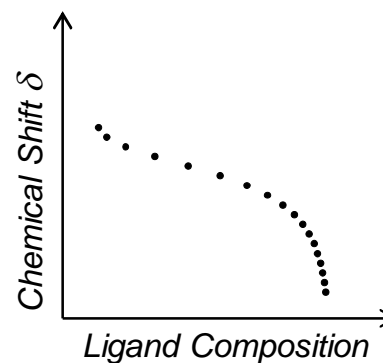
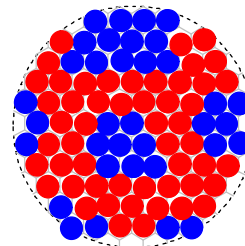
Janus

$$\delta = \delta_B + \frac{(\delta_I - \delta_B)t}{2rx_A}$$



Patches

$$\delta = f(\delta_B, \delta_I, x_A)$$

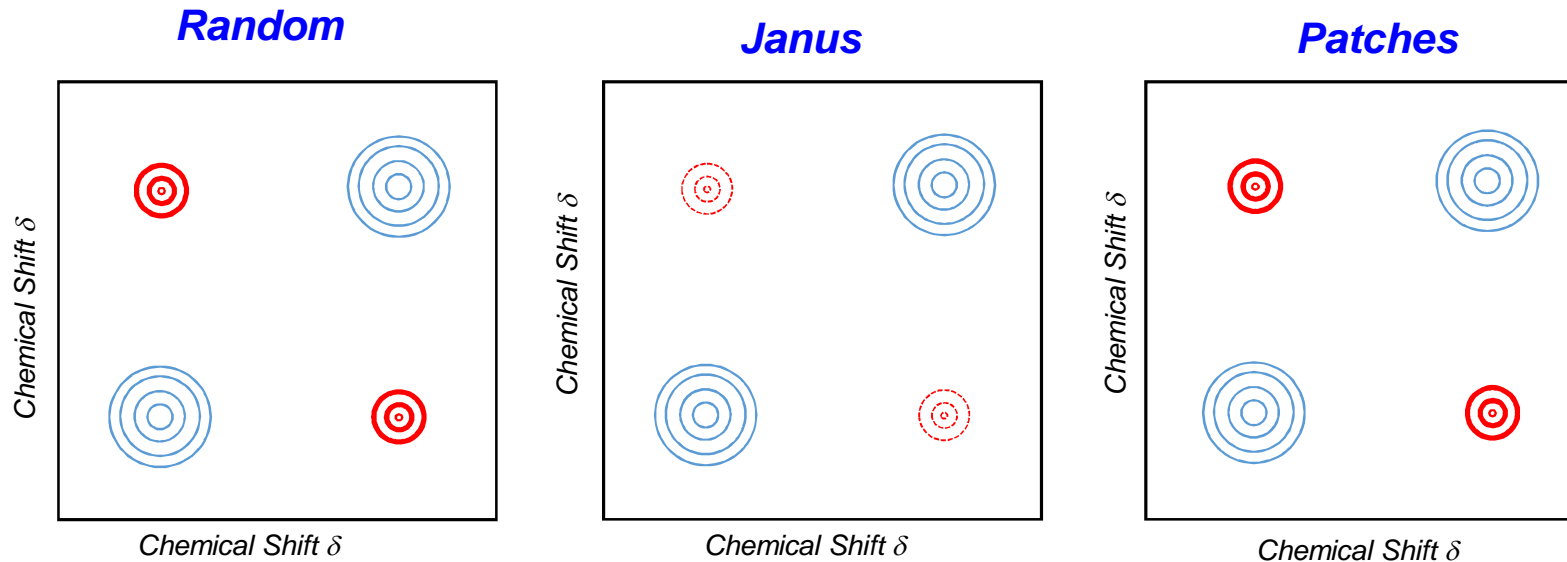


δ_B chemical shift in the bulk
 δ_I chemical shift at interface
 x_A composition of the NP
 r NP core radius
 t thickness of the stripe

Predicted NMR patterns for nanoparticles coated with a binary mixture of ligands

NOESY - atoms of ligands that are in close proximity to each other can give a NOE

distance between groups smaller than 0.4 nm

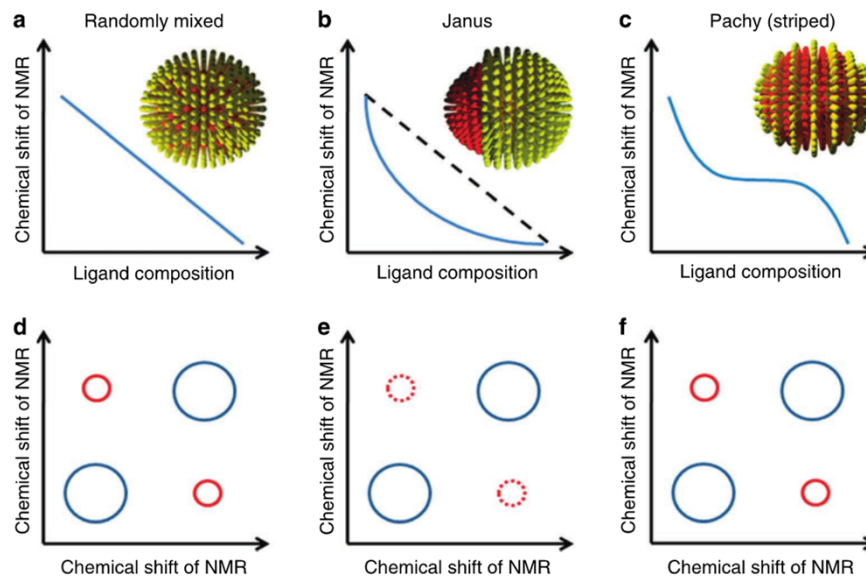
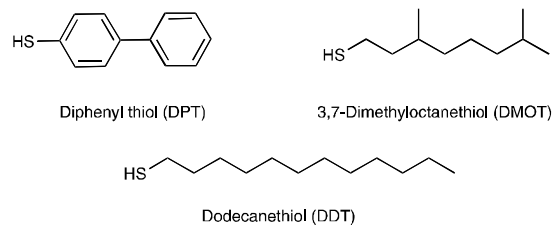


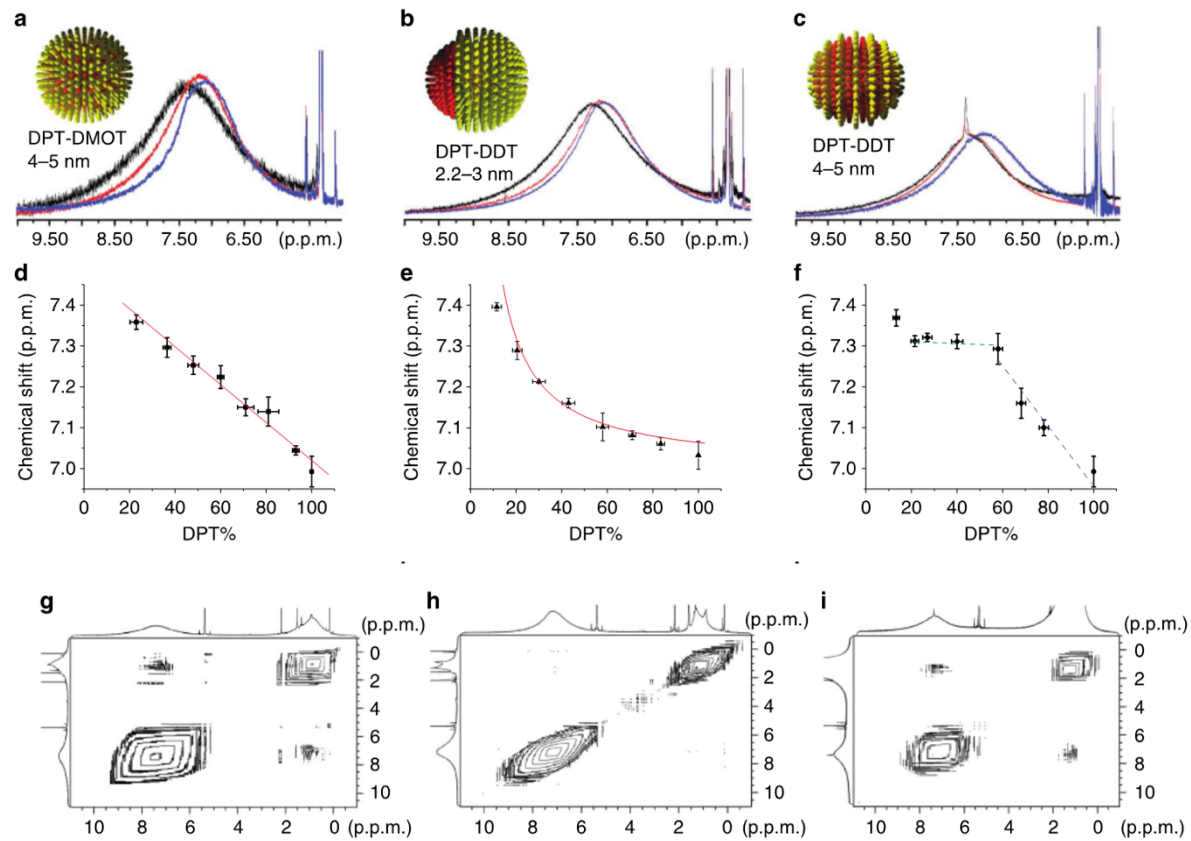
S. Pradham, L. E. Brown, J. P. Konopelski, S. Chen *J. Nanopart. Res.* **2009**, 11, 1895.
X. Liu, M. Yu, H. Kim, M. Mameji, F. Stellacci *Nature Commun.* **2012**, 3, 1182.

Determination of monolayer-protected gold nanoparticle ligand-shell morphology using NMR

Xiang Liu¹, Miao Yu¹, Hyewon Kim², Marta Mameli¹ & Francesco Stellacci¹

Nature Commun. 2012





Lanthanide-Based NMR: A Tool To Investigate Component Distribution in Mixed-Monolayer-Protected Nanoparticles

Gaetano Guarino, Federico Rastrelli,* Paolo Scrimin, and Fabrizio Mancin*

J. Am. Chem. Soc. 2012, 134, 7200–7203

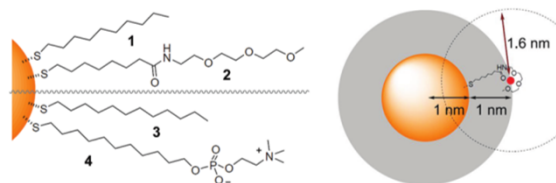


Figure 1. (Left) Nanoparticle-bound coating thiols used in this work. (Right) Schematic Gd³⁺ (red dot) binding site for thiol **2**-coated NPs (only one thiol is represented for simplicity, but cooperative binding by multiple thiols is likely to occur), and metal ion "quenching radius" (dashed line).

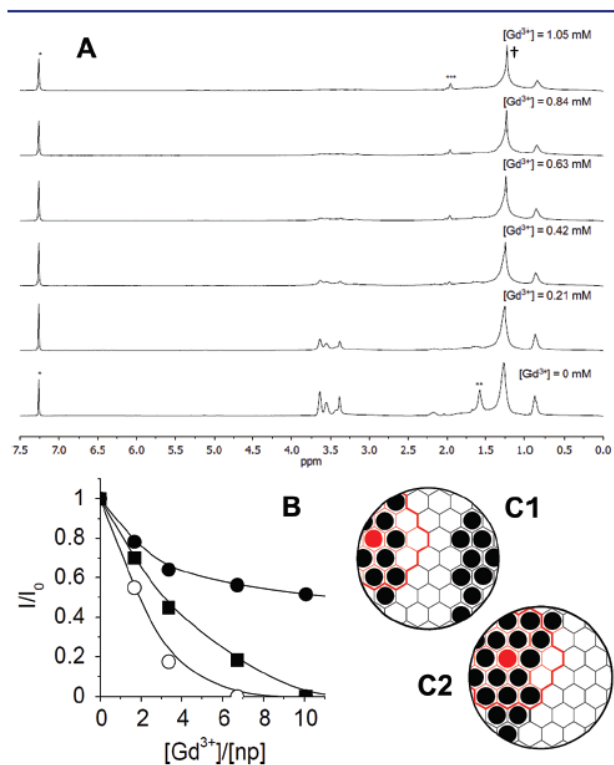


Figure 4. (A) ^1H NMR spectra of a CDCl_3 solution of gold nanoparticles coated with a mixed monolayer of thiols 1 and 2 in a 50:50 ratio ($[1] = [2] = 5 \text{ mM}$, $[\text{NP}] = 0.14 \text{ mM}$) recorded upon addition of increasing amounts of a CD_3CN solution of $\text{Gd}(\text{CF}_3\text{SO}_3)_3$ (*, residual solvents; **, water; ***, CH_3CN ; †, Gd^{3+} impurity). (B) Relative intensity of signals from thiols 1 (●, peak at 0.8 ppm) and 2 (○, peak at 2.1 ppm) as a function of the Gd^{3+} ions/particles ratio (lines, data trend; ■, data from Figure 2B for 100% 2-coated NPs). (C) Schematic interpretation of the experiment: Gd^{3+} ions (red circles) bind to thiols 2 (filled hexagons), which are grouped in patches on the surface of the NPs; as a consequence, only signals from thiols 2 are canceled, while thiols 1 are marginally affected.

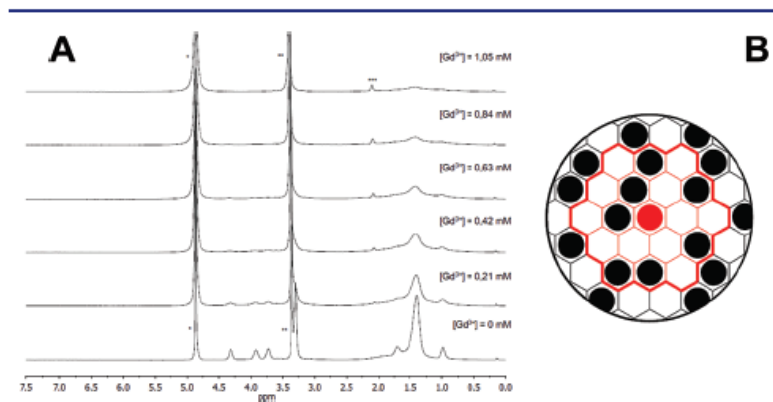


Figure 5. (A) ^1H NMR spectra of a CD_3OD solution of gold nanoparticles coated with a 1:1 mixture of thiols 3 and 4 ($[3] = [4] = 5 \text{ mM}$, $[\text{NP}] = 0.14 \text{ mM}$) recorded upon addition of increasing amounts of a CD_3CN solution of $\text{Gd}(\text{CF}_3\text{SO}_3)_3$ (*, methanol $-\text{OH}$; **, methanol $-\text{CHD}_2$; ***, CH_3CN). (B) Schematic interpretation of the experiment: Gd^{3+} ions (red circles) bind to thiols 4 (filled hexagons) on the surface of the NPs, canceling the signals of both thiols 3 and 4 that are randomly distributed.

Scanning tunneling microscopy and small angle neutron scattering study of mixed monolayer protected gold nanoparticles in organic solvents†

Mauro Moglianetti,^{‡a} Quy Khac Ong,^{‡a} Javier Reguera,^{‡a} Kellen M. Harkness,^a Marta Mameli,^a Aurel Radulescu,^b Joachim Kohlbrecher,^c Corinne Jud,^d Dmitri I. Svergun^{*e} and Francesco Stellacci^{*a}

Chem. Sci., 2014, 5, 1232

Table 1 Contrasts of the phases in the hybrid particles (in units 10^{-6} \AA^{-2}) (a) and discrepancy of the fits (b)

(a) Contrasts	C6 : d-C12	d-C6 : C12
Phase 1 : gold	1.4	1.4
Phase 2 : C12	2.5	-3.4
Phase 3 : C6	-3.4	1.9
(b) Discrepancy values ^a	C6 : d-C12	d-C6 : C12
Striped particle	1.2	1.1
Janus particle	15.2	7.7
Randomly mixed particles	1.8	4.2

^a Chi squared.

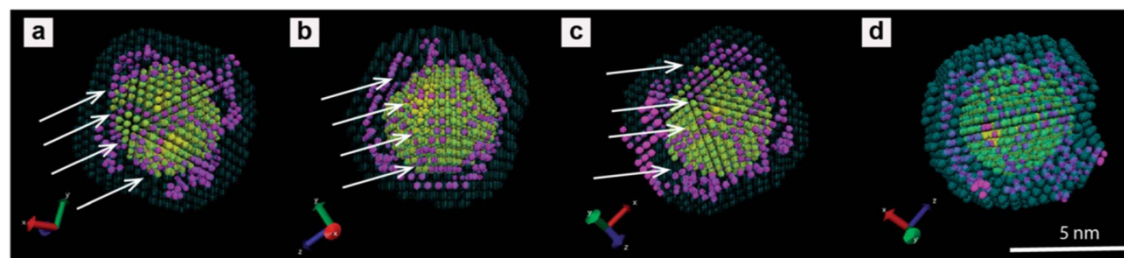


Fig. 5 Four different projections of a typical multiphase 3D low-resolution model of the C6 : C12 particles obtained from the fitting of the SANS data. Yellow beads indicate the gold nanoparticle core regions, the magenta beads represent the C6 moiety, and the cyan beads the C12 moiety. The beads in the model act as low-resolution place holders to depict the space occupied by the gold, C6 and C12 moieties. The image (d) on the right has the cyan beads in a lower transparency mode to highlight the C12 moieties. The C6 regions form elongated domains within the bulk of the C12 phase in excellent agreement with the model of striped nanoparticles. Scale bar, 5 nm. The arrows indicate elongated C6 domains that roughly align along a preferential direction. These features would provide aligned domain boundaries in the STM images (the arrows are spaced by about 1 nm).

MALDI-MS investigation of molecular phase separation in mixed ligand coated NP

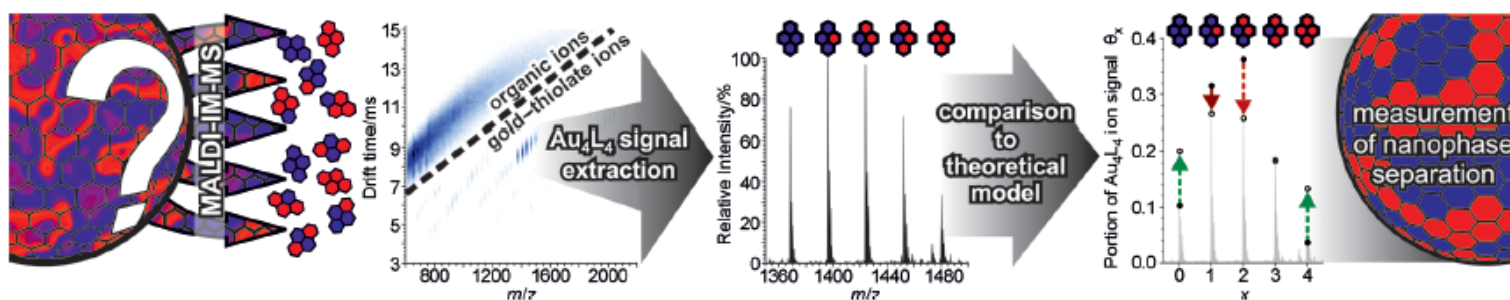
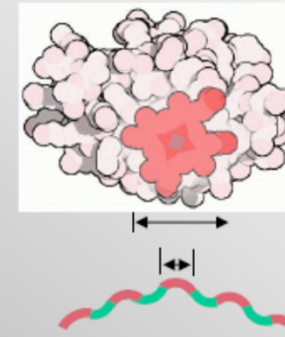
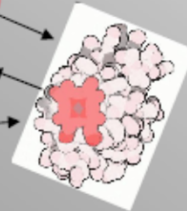
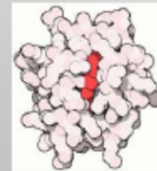
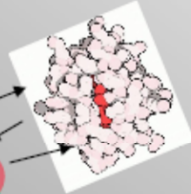
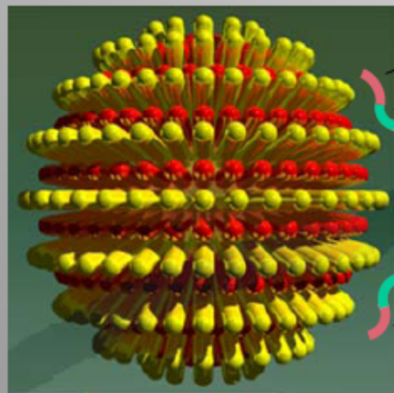
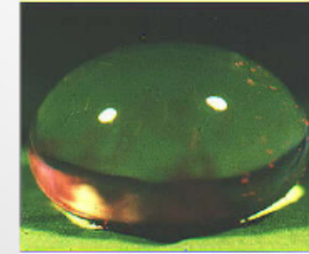


Figure 1. Typical workflow for experiments presented here. Mixed-ligand AuNPs with unknown levels of nanophase separation are analyzed by MALDI-IM-MS. The MALDI process leads to the fragmentation of protecting gold-thiolate complexes from the AuNP surface. The gold-thiolate ions undergo gas-phase separation from organic ions. The Au₄L₄ ion species are extracted from the data by software, and their abundances are compared to a theoretical model based on the binomial distribution. Deviations indicate nanophase separation in the AuNP monolayer.

Harkness, K. M.; Balinski, A.; McLean, J. A.; Cliffler, D. E. s. *Angew. Chem., Int. Ed.* 2011, 50, 10554–10559

The Nano Lotus Leaf Effect



Size of hydrophobic/hydrophilic regions of protein are greater than size scale of ligand domains on the nanoparticles.

Proteins are **conformationally frustrated** and cannot adsorb to nanoparticle surface.

Molecular Dynamics Simulation Study of Self-Assembled Monolayers of Alkanethiol Surfactants on Spherical Gold Nanoparticles[†]

Pradip Kr. Ghorai[‡] and Sharon C. Glotzer

15858 *J. Phys. Chem. C, Vol. 111, No. 43, 2007*

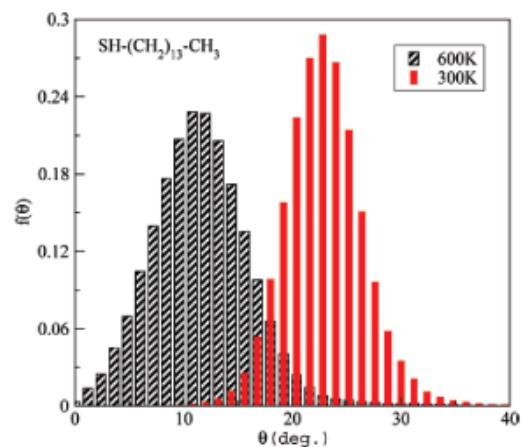


Figure 2. Distribution of tilt angle for 13-carbon alkanethiols on a Au(111) surface at 300 (rightmost data) and 600 K (leftmost data).



Figure 3. Snapshots of alkanethiol $[\text{SH}-(\text{CH}_2)_{13}-\text{CH}_3]$ SAMs from our MD simulations at (a) 300 and (b) 600 K.

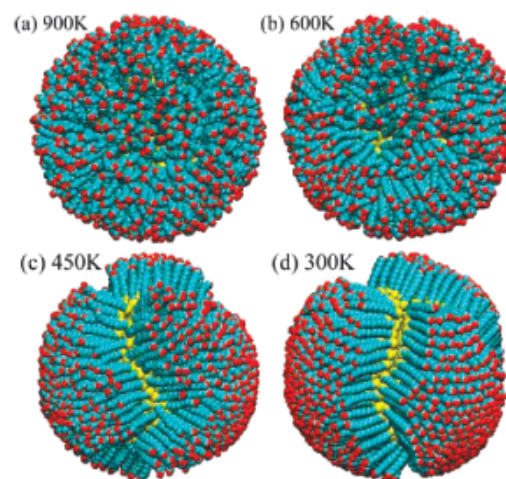


Figure 4. Snapshots of homoligand alkanethiol $[\text{SH}-(\text{CH}_2)_{13}-\text{CH}_3]$ SAMs from our MD simulations at (a) 900, (b) 600, (c) 450, and (d) 300 K. Disclination lines arise due to the curvature of the surface.³⁶

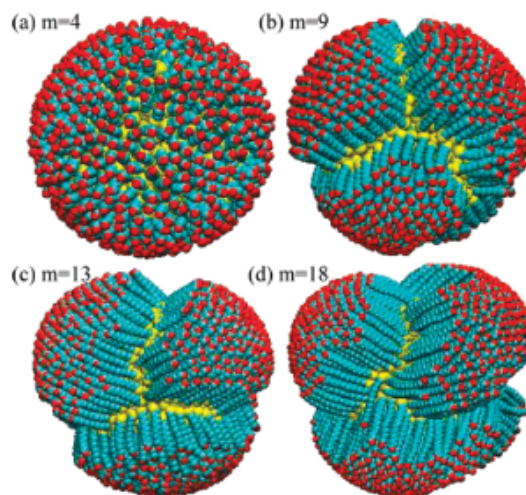


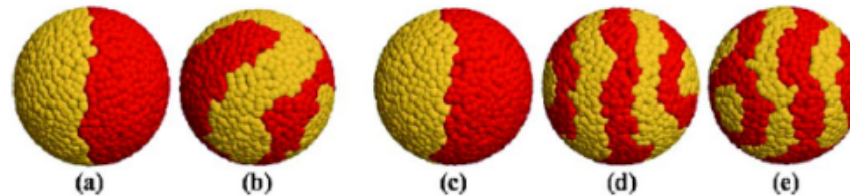
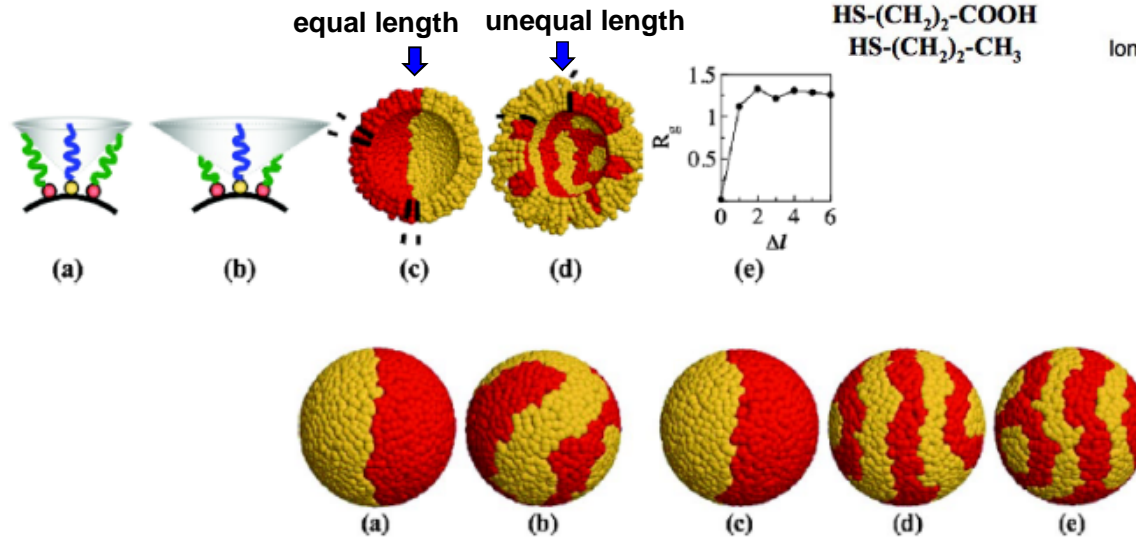
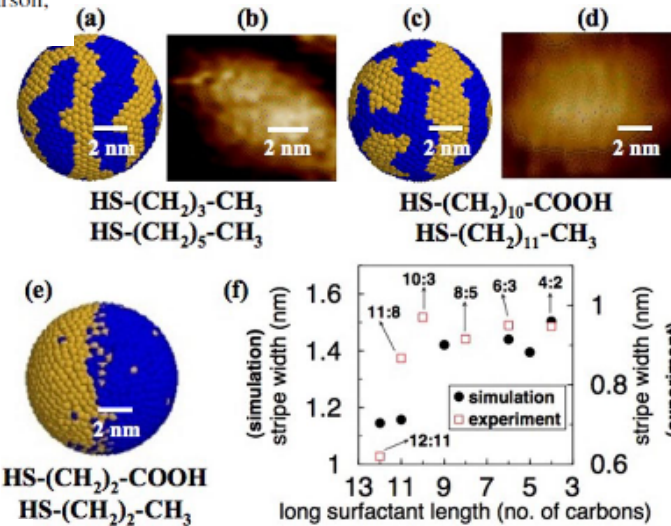
Figure 6. Snapshots of homoligand alkanethiol $[\text{SH}-(\text{CH}_2)_m-\text{CH}_3]$ SAMs for different tail lengths; (a) $m = 4$, (b) $m = 9$, (c) $m = 13$, and (d) $m = 18$ at 300 K.

Entropy-Mediated Patterning of Surfactant-Coated Nanoparticles and Surfaces

Chetana Singh,¹ Pradip K. Ghorai,¹ Mark A. Horsch,¹ Alicia M. Jackson,² Ronald G. Larson,¹
 Francesco Stellacci,² and Sharon C. Glotzer^{1,3,*}

PRL 99, 226106 (2007)

AuNP 7.0 nm in diameter



(a) Length ratio 4:4, equal bulkiness. (b) Length ratio 6:6 with one surfactant (yellow heads) having a bulkier tail group. (c)–(e) Length ratios 4:6, 4:7 and 4:13, respectively, with equal bulkiness.

Exploiting Substrate Stress To Modify Nanoscale SAM Patterns

Chetana Singh,[†] Alicia M. Jackson,[‡] Francesco Stellacci,[‡] and Sharon C. Glotzer^{*†}

J. AM. CHEM. SOC. 2009, 131, 16377–16379

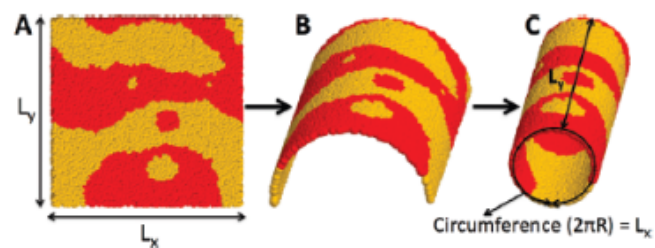
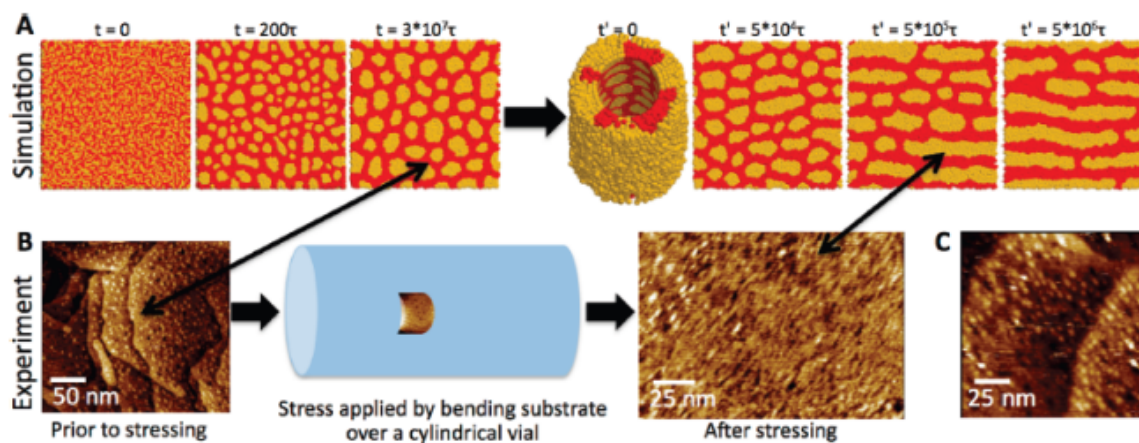
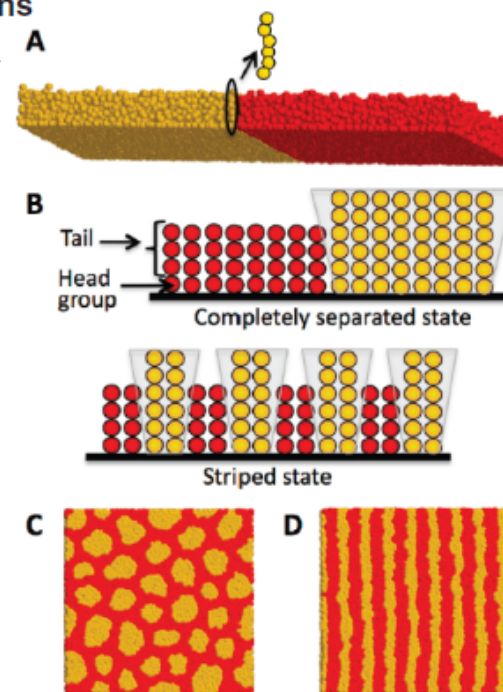
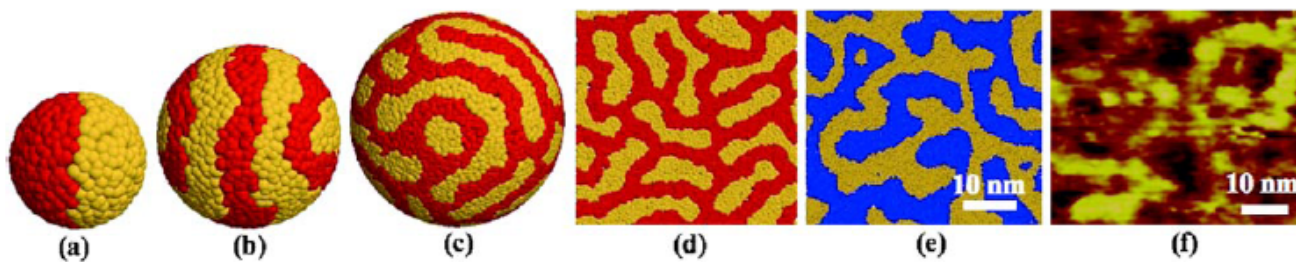
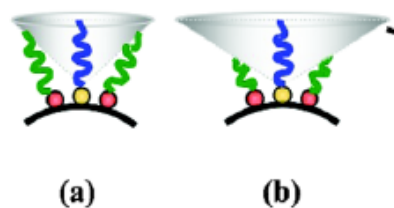
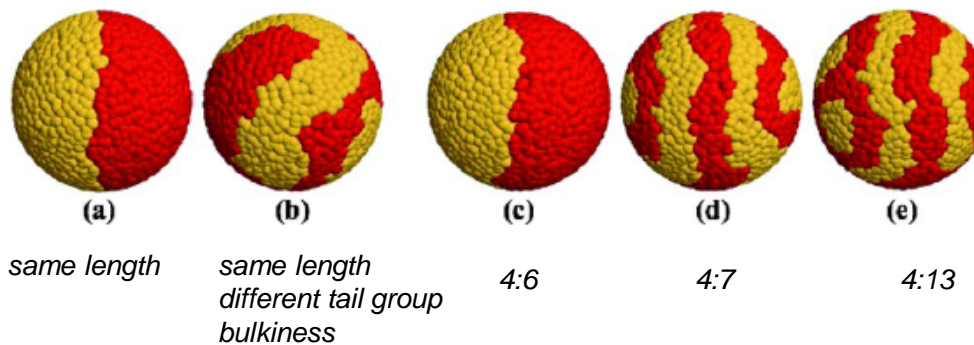


Figure 1. Transfer of an arbitrary pattern from a flat surface onto a cylinder. (A) Starting pattern on flat surface. (B) Intermediate curved surface. (C) Final pattern on cylindrical surface.



morphologies of mixed-monolayers

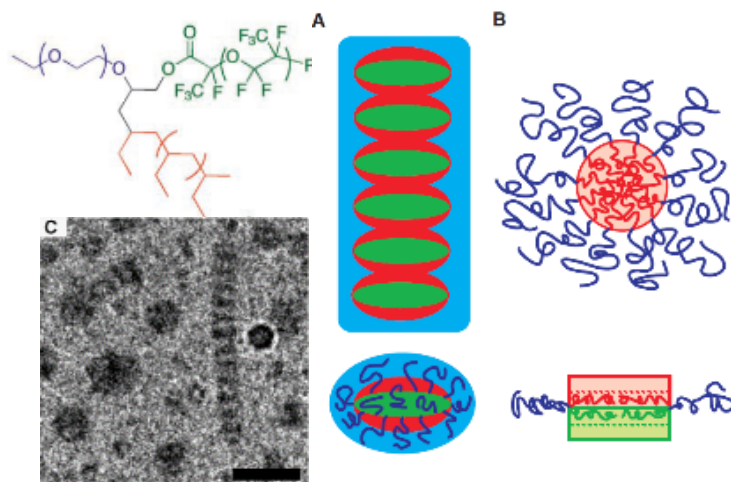
Entropy-Mediated Patterning of Surfactant-Coated Nanoparticles and Surfaces



surfaces with varying degrees of curvature, different length C4:C6,
same end group.

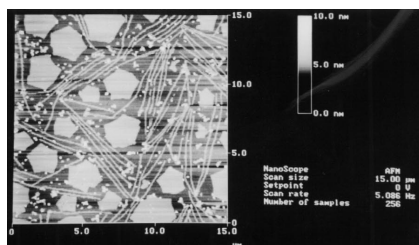
phase segregation of hydrogenated/fluorinated units

block terpolymer



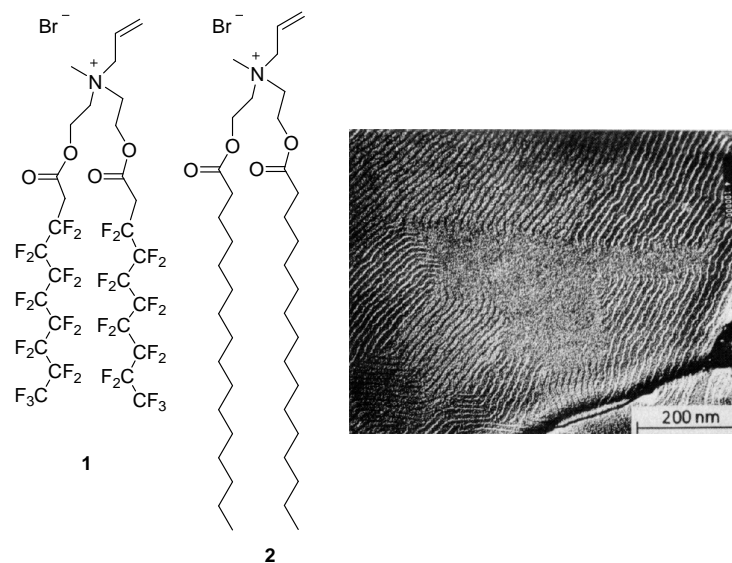
T. P. Lodge et al. *Science* **2004**, 306, 98

monolayers



AFM images of a mixed monolayer of 1:1 $C_{18}H_{37}SO_3Na-C_8F_{17}COOH$ deposited on a freshly cleaved mica surface at a compression rate of $35 \text{ cm}^2 \text{ min}^{-1}$. *Coll. Surf. A*, **1999**, 157, 63-71.

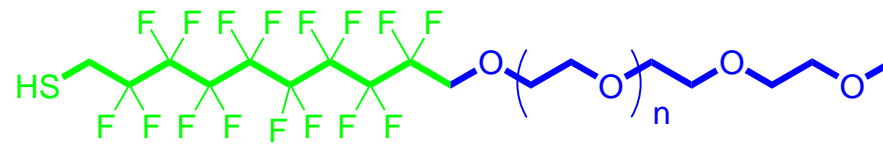
Liposomes



Freeze fracture electron micrograph of a phase-separated liposomal membrane (95 mol % **DMPC** and 5 mol % fluorinated lipid **3**). The ripple structure shows the parts of membrane composed of DMPC, surrounding a domain of the fluorinated lipid (smooth surface). R. Elbert, T. Folda, and H. Ringsdorf *J. Am. Chem. Soc.* **1984**, 106, 7687-1692

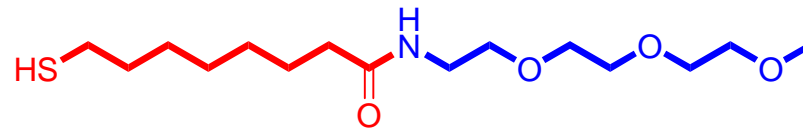
organization of mixed - monolayers

3D SAMs composed of thiols with immiscible chains



n = 8,9

HS-F8-PEG



HS-C8-TEG

ESR Spectroscopy as a tool to investigate the monolayer properties

AuNPs protected by perfluorinated amphiphilic thiolates

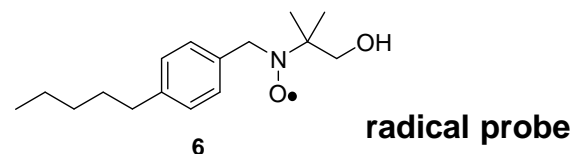
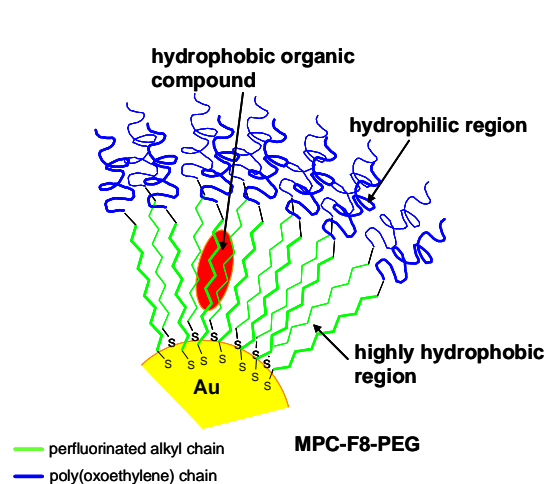
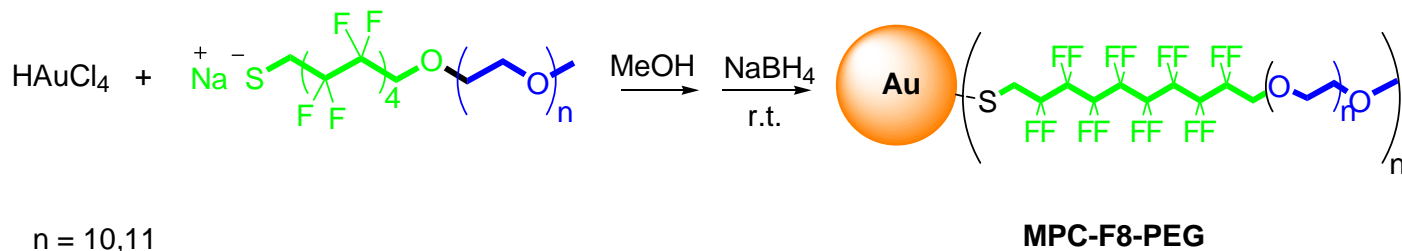


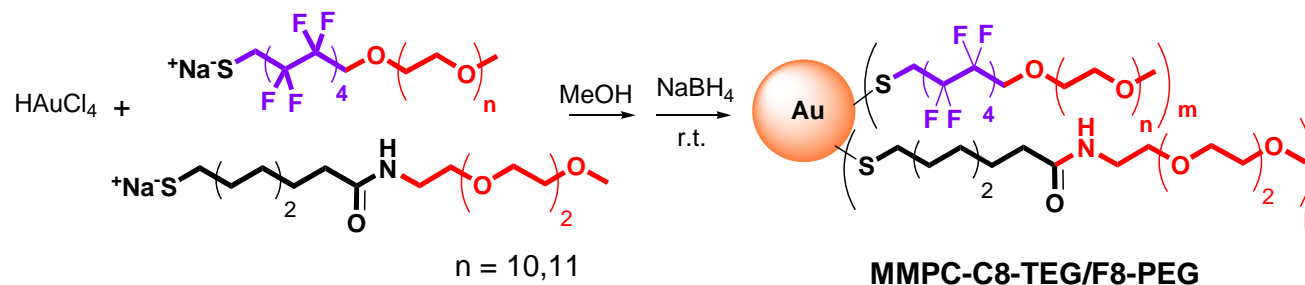
Table 1. ESR Parameters of **6** (1 G = 0.1 mT) and Partition Equilibrium (K_{eq}) Constants at 298 K

	$a(\text{N})/\text{G}$	$a(2\text{H}_\beta)/\text{G}$	g -factor	$K_{\text{eq}}/\text{M}^{-1}$
water ^a	16.25	10.14	2.0056	—
MPC-F8-TEG	15.46	8.68	2.0057	176
MPC-C8-TEG ^b	15.67	8.97	2.0057	87 ^c

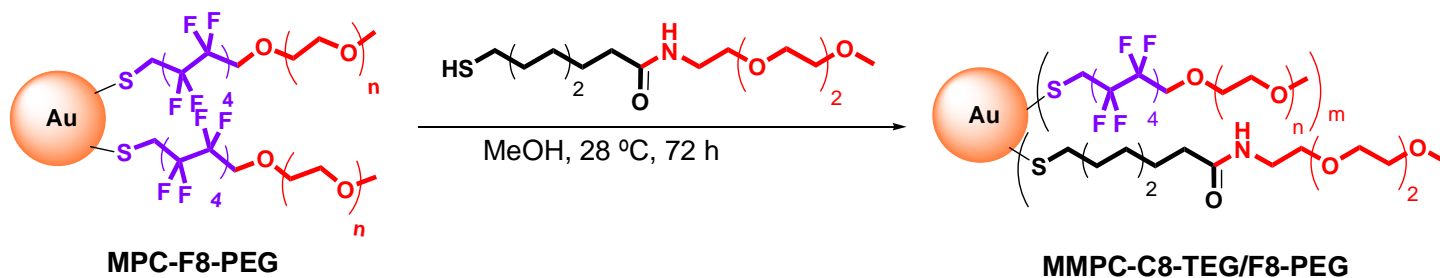
^a Contains 10% (v/v) of methanol. ^b From ref 27. ^c See ref 33.

gold nanoparticles protected by H-/F- mixed-monolayers

- Homogeneous phase synthesis (methanol/water) using mixtures of thiolates with **immiscible chains**



- synthesis of mixed-monolayer by exchange reaction



C. Gentilini, P. Franchi, E. Mileo, S. Polizzi, M. Lucarini, L. Pasquato *Angew. Chem. Int. Ed.* **2009**, 48, 3060.

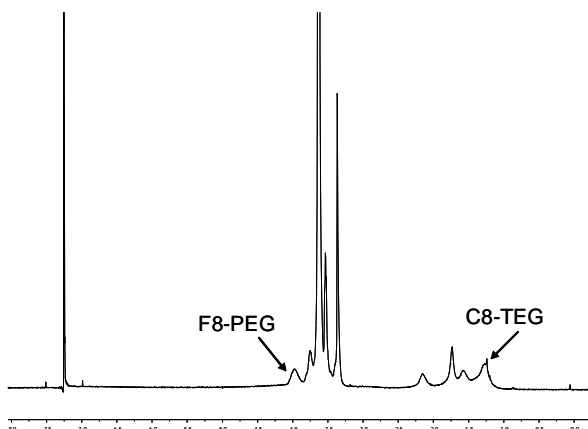
water-soluble perfluoro GNPs

Table 1: Gold nanoparticles coated with mixtures of thiolates of **1** and **2**.

Sample	R _{SAM} ^[a]	Core diameter ^[b] (nm)	% Organic ^[c]	MPC composition ^[d]
1	1	2.2 ± 0.4	47	Au ₄₀₀ (SC8TEG) ₅₄ (SF8PEG) ₅₄
2 ^[e]	1	1.6 ± 0.2	59	Au ₁₅₀ (SC8TEG) ₃₃ (SF8PEG) ₃₃
3	2.5	2.5 ± 0.4	42	Au ₅₄₀ (SC8TEG) ₁₀₈ (SF8PEG) ₄₃
4	4	1.9 ± 0.2	45	Au ₂₃₀ (SC8TEG) ₆₆ (SF8PEG) ₁₆
5	20	1.9 ± 0.3	35	Au ₂₄₀ (SC8TEG) ₆₈ (SF8PEG) ₃

[a] Ratio of the two thiols forming the monolayer determined by integration of ¹H NMR signals pertaining to thiol **1** and to thiol **2** in the nanoparticles. [b] Average core diameter by TEM measurements of at least 300 NPs. [c] Determined by TGA. [d] Estimated composition based on TEM and TGA analysis and considering R_{SAM}. [e] Prepared from MPC-F8-PEG by place-exchange procedure.

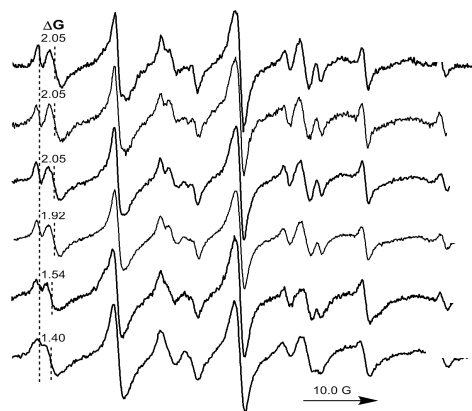
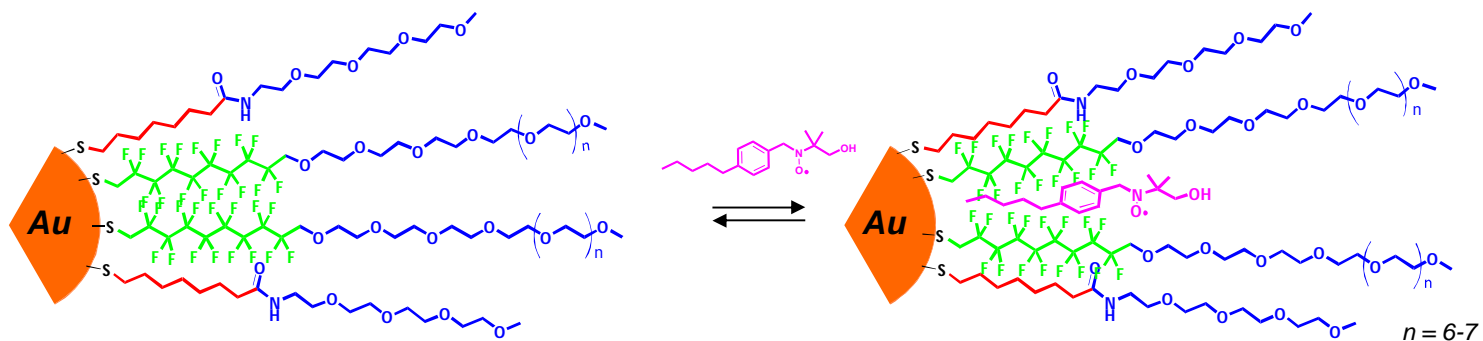
$$R_{\text{SAM}} = \text{H-thiol}/\text{F-thiol}$$



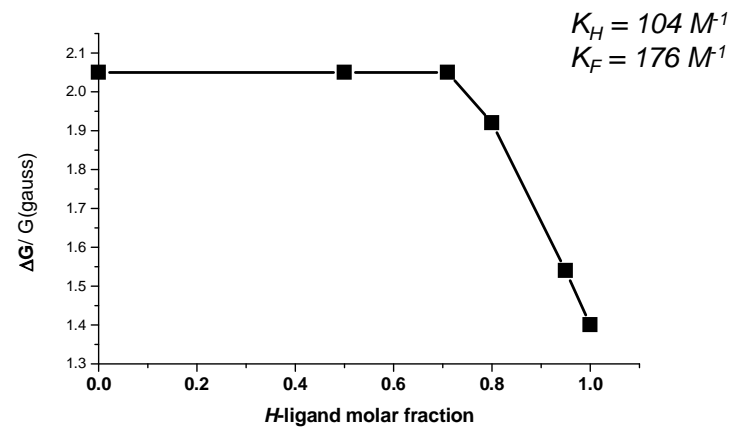
¹H-NMR (CDCl₃, 400 MHz) of MMPC-C8-TEG/F8-PEG.

C. Gentilini, P. Franchi, E. Mileo, S. Polizzi, M. Lucarini, L. Pasquato *Angew. Chem. Int. Ed.* **2009**, *48*, 3060.

gold nanoparticles protected by H-/F- mixed-monolayers

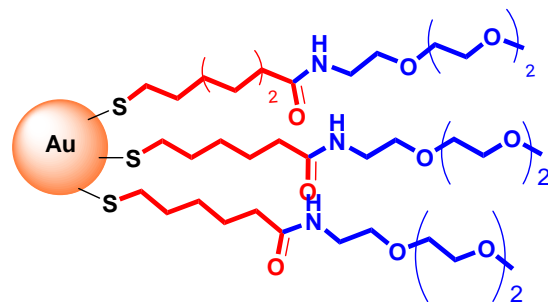


MPC-F8-PEG
 $R_{SAM} 1$
 $R_{SAM} 2.5$
 $R_{SAM} 4$
 $R_{SAM} 20$
 MPC-C8-TEG

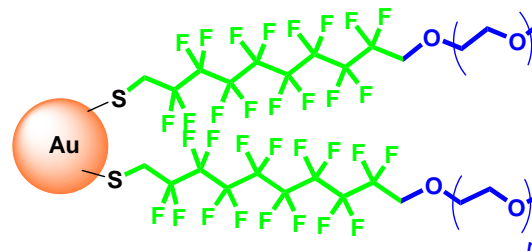


C. Gentilini, P. Franchi, E. Mileo, S. Polizzi, M. Lucarini, L. Pasquato *Angew. Chem. Int. Ed.* **2009**, 48, 3060.

water-soluble perfluoro GNPs

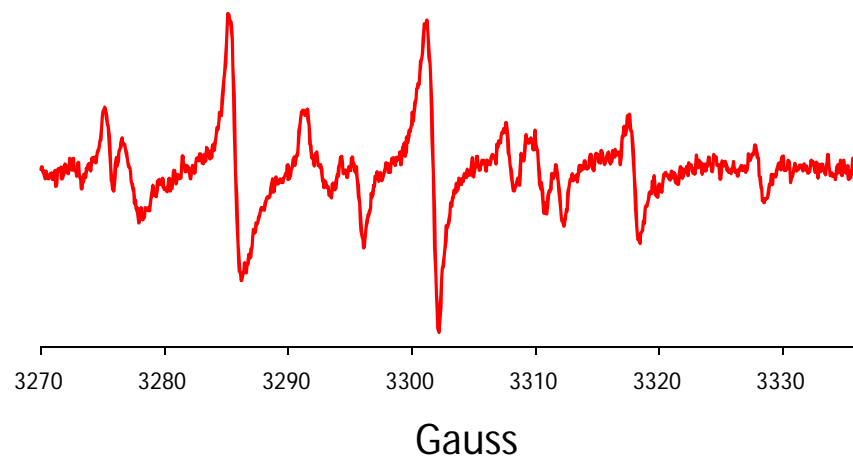


MPC-C8-TEG



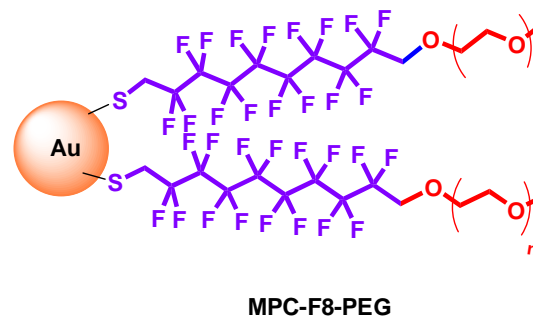
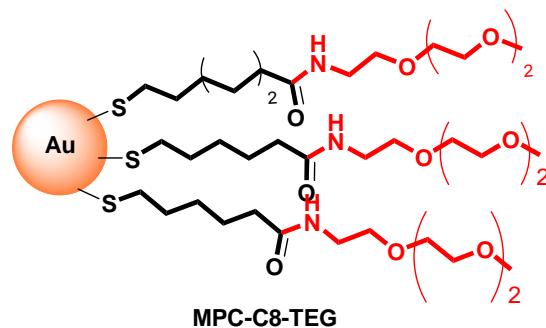
MPC-F8-PEG

$$[\text{C8-TEG}] / [\text{F8-PEG}] = 1/1, \Delta G = 1.91$$



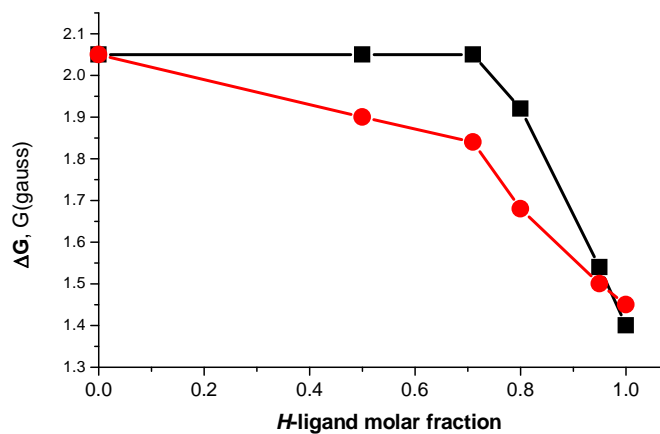
mixed-monolayers are formed
mixture of two population of homoligand NPs can be ruled out

gold nanoparticles protected by H-/F- mixed-monolayers



ESR Parameters in the Presence of Homoligand NP Mixtures

χ	$\Delta G/G$	
0	2.05	2.05
0.5	2.05	1.90
0.71	2.05	1.84
0.80	1.92	1.68
0.95	1.54	1.50
1	1.40	1.45



P. Posocco, C. Gentilini, S. Bidoggia, A. Pace, P. Franchi, M. Lucarini, M. Fermeglia, S. Pricl, L. Pasquato, ACS Nano 2012, 6, 7243-7253.

gold nanoparticles protected by H-/F- mixed-monolayers

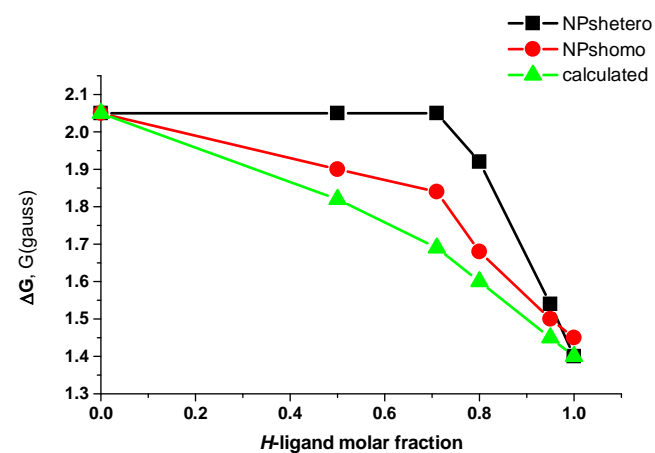
$$\Delta G = 1.40X_H + 2.05(1 - X_H)$$

$$X_H = \frac{\frac{K_H[H\text{-ligand}]}{K_F[F\text{-ligand}]}}{1 + \frac{K_H[H\text{-ligand}]}{K_F[F\text{-ligand}]}}$$

$$K_H = 104 \text{ M}^{-1}$$

$$K_F = 176 \text{ M}^{-1}$$

χ	$\Delta G/G$		
	HeteroL	HomoL	calcd.
0	2.05	2.05	2.05
0.5	2.05	1.90	1.82
0.71	2.05	1.84	1.69
0.80	1.92	1.68	1.60
0.95	1.54	1.50	1.45
1	1.40	1.45	1.40



water-soluble perfluoro GNPs – organization of the monolayer

atomistic and mesoscale calculations

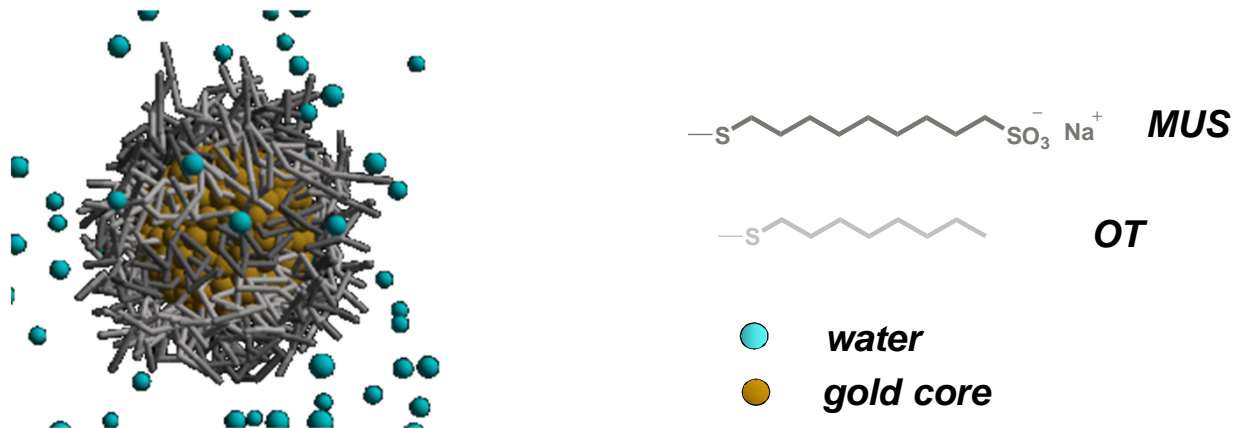
- Models of the NPs were obtained employing an innovative **multiscale molecular simulation** approach
- This approach combines **mesoscale techniques**, developed to describe systems with properties at the nanometer scale, and **atomistic techniques**, which model matter at the level of atoms
- In particular, morphological characterization of the NPs was predicted using mesoscale models (Dissipative Particle Dynamics), whose chemical potentials were derived from simulations at a lower level of detail (Molecular Dynamics)
- Simulation have been carried out in the presence of water as solvent, at 298 K, and considering the mobility of the thiolates on the gold surface

P. Posocco, C. Gentilini,[†] S. Bidoggia, A. Pace, P.Franchi, M. Lucarini, M. Fermeiglia, S. Pricl, L. Pasquato
ACS Nano **2012**, 6, 7243.

gold nanoparticles protected by H-/F- mixed-monolayers

■ multiscale molecular simulation: validation of the procedure

Au NP with a core size of 4.5 nm coated by a mixture of 2:1 of MUS and OT ligands (F. Stellacci et al. Chem. Commun. 2008, 196.)



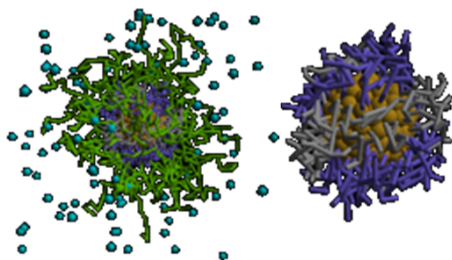
Rippled morphology predicted using a multiscale approach.

L. Pasquato, et. al. ACS Nano **2012**, 6, 7243-7253.

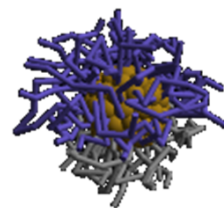
gold nanoparticles protected by H-/F- mixed-monolayers

■ multiscale molecular simulation

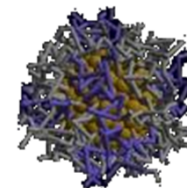
Ligand organization on the surface of gold NPs at different molar fraction of the two ligands



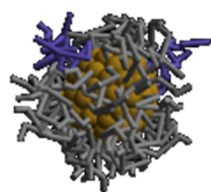
$\chi_H = 0.50$, $\varnothing 2.2$ nm



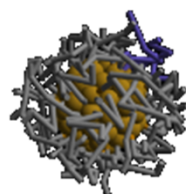
$\chi_H = 0.50$, $\varnothing 1.6$ nm



$\chi_H = 0.71$, $\varnothing 2.5$ nm

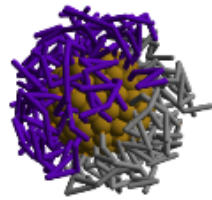


$\chi_H = 0.80$, $\varnothing 1.9$ nm

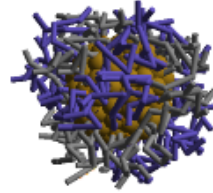


$\chi_H = 0.95$, $\varnothing 1.9$ nm

L. Pasquato, et al. ACS Nano **2012**, 6, 7243-7253.

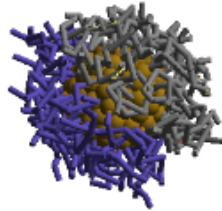


S1C3 S1F3

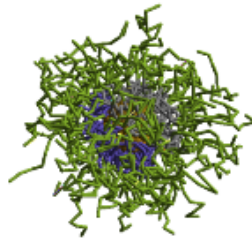


S1C3 S1F4

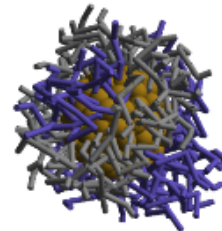
gold core \varnothing 2.2 nm
54 **H** chains (bead C)
54 **F** chains (bead F)
bead P is for PEG
bead S is for Sulfur



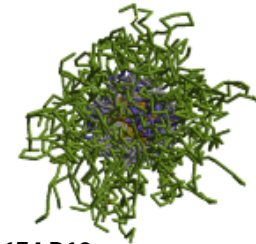
S1C3 P10



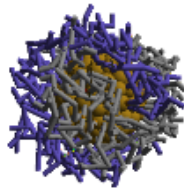
S1 F3 P10



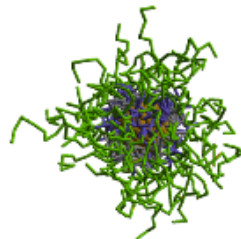
S1C3 P10



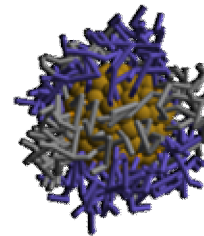
S1F4 P10



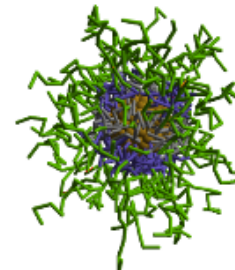
S1 C3 P2



S1 F3 P10



S1C3 P2



S1F4 P10

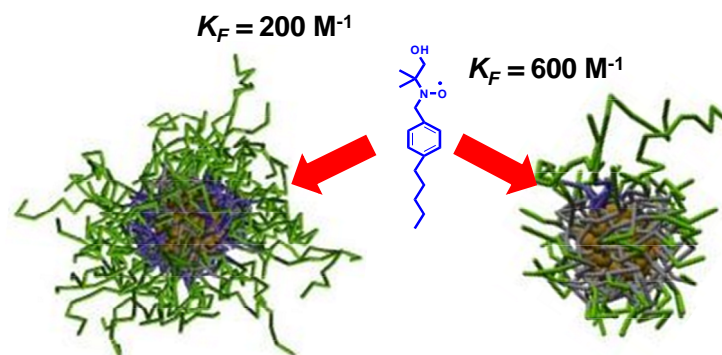


TABLE 2. Equilibrium Constants ($T = 298 \text{ K}$) and ESR Parameters in the Presence of Heteroligand Mixed Monolayers

χ	$K_{\text{mix}}/\text{M}^{-1}$	$\Delta G/G^d$	K_H/K_F^e	K_F/M^{-1}	K_H/M^{-1}
0	176 ^d	2.05 (2.05)		176 ^d	
0.50	100 ± 7.7 ^b	2.05 (1.82)	<0.04	200	<10
0.71	100 ± 8.1	2.05 (1.69)	<0.04	350	<10
0.80	189 ± 20	1.92 (1.60)	0.06	762 ^f	45 ^f
0.95	120 ± 11	1.54 (1.45)	0.16	600 ^f	96 ^f
1	104 ^c	1.40 (1.40)			104 ^c

^aFrom ref 26. ^bErrors refer to twice the standard deviation. ^cFrom ref 25.

^dDetermined by ESR. In parentheses the theoretical value calculated by using eqs 1 and 2 with $K_H/K_F = 0.59$. ^eDetermined by the experimental values of ΔG .

^fDetermined by solving eqs 1, 3, and 4, simultaneously.

gold nanoparticles protected by H-/F- mixed-monolayers

Equilibrium constants (T = 298 K) in the presence of Heteroligand mixed-monolayers

χ	$K_{\text{mix}}/\text{M}^{-1}$	$K_{\text{H}}/K_{\text{F}}^e$	$K_{\text{F}}/\text{M}^{-1}$	$K_{\text{H}}/\text{M}^{-1}$
0	176 ^d		176 ^d	
0.50	100 ± 7.7 ^b	<0.04	200	<10
0.71	100 ± 8.1	<0.04	350	<10
0.80	189 ± 20	0.06	762 ^f	45 ^f
0.95	120 ± 11	0.16	600 ^f	96 ^f
1	104 ^c			104 ^c

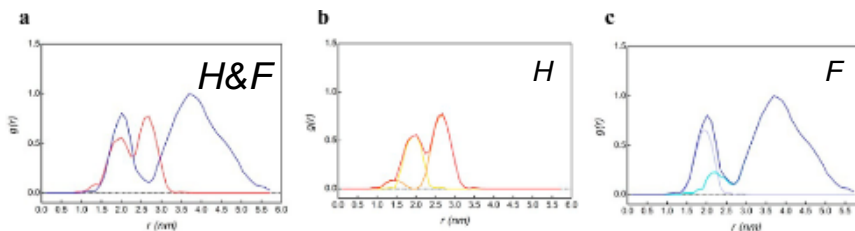
shell thickness | F8PEG 2.82 nm in
homoligand NPs

| C8TEG 1.40 nm

heteroligand NPs

| F8PEG 2.60 nm in

| C8TEG 1.59 nm



Radial distribution functions (RDFs) for the SAM components of MPC-C8-TEG/F8-PEG, 1:1

