

ITC XXVIII - Nanoparticles studies

Agrawal V. V., Varghese N., Kulkarni G. U. and Rao C. N. (2008) Effects of changes in the interparticle separation induced by alkanethiols on the surface plasmon band and other properties of nanocrystalline gold films. *Langmuir* **24**, 2494-2500.

Abstract: Effects of changing the interparticle separation on the surface plasmon bands of ultrathin films of gold nanoparticles have been investigated by examining the interaction of alkanethiols of varying chain length on nanocrystalline gold films generated at the organic-aqueous interface. Adsorption of alkanethiols causes blue-shifts of the surface plasmon adsorption band, the magnitude of the shift being proportional to the chain length. The disordered nanocrystals thus created (λ_{damax} , 530 nm) are in equilibrium with the ordered nanocrystals in the film (λ_{damax} , 700 nm) as indicated by an isosbestic point around 600 nm. Long chain thiols disintegrate or disorder the gold films more effectively, as demonstrated by the increased population of the thiol-capped gold nanocrystals in solution. The rate of interaction of the thiols with the film decreases with the decreasing chain length. The effect of an alkanethiol on the spectrum of the gold film is specific, in that the effects with long and short chains are reversible. The changes in the plasmon band of gold due to interparticle separation can be satisfactorily modeled on the basis of the Maxwell-Garnett formalism. Spectroscopic studies, augmented by calorimetric measurements, suggest that the interaction of alkanethiols involves two steps, the first step being the exothermic gold film-thiol interaction and the second step includes the endothermic disordering process followed by further thiol capping of isolated gold particles

Barbosa M. E., Bouteiller L., Cammas-Marion S., Montembault V., Fontaine L. and Ponchel G. (2008) Synthesis and ITC characterization of novel nanoparticles constituted by poly(γ -benzyl L-glutamate)- β -cyclodextrin. *J Mol Recognit* **21**, 169-178.

Abstract: Imparting desired technological characteristics to polymeric nanoparticles requires the development of original polymers. In the present work, the synthesis and characterization of a novel PBLG-derivative, the poly(γ -benzyl L-glutamate)- β -cyclodextrin (PBLG- β -CD-50), have been carried out. Nanoparticles from either PBLG- β -CD-50 polymer or from mixtures with PBLG have been prepared using a modified nanoprecipitation method. Spherically shaped nanoparticles with diameter in the range of 50-70 nm were obtained, as determined by dynamic laser light scattering and transmission electron microscopy. The presence of a surfactant in the suspension medium had almost no influence on these parameters and was not necessary to the shelf-stability of the suspension. Further, isothermal titration microcalorimetry (ITC) experiments have been used to show unambiguously that about 20% of the cyclodextrins remain functional within the particles. Consequently, this system may be of interest when association of large amounts of hydrophobic drugs to nanoparticles is required

Bouchemal K. (2008) New challenges for pharmaceutical formulations and drug delivery systems characterization using isothermal titration calorimetry. *Drug Discov. Today* **13**, 960-972.

Abstract: Long viewed as the 'method of choice' for characterizing thermodynamics and stoichiometry of molecular interactions, with high sensitivity, isothermal titration calorimetry (ITC) has been applied to many areas of pharmaceutical analysis. This review highlights ITC employment to measure binding thermodynamics and their use for pharmaceutical formulations and drug delivery system characterization particularly cyclodextrin-guest interactions, investigation of micellar-based systems, polyelectrolytes, nucleic acid interactions with multivalent cations and the optimization of DNA targeting and delivery. Furthermore, the potential of ITC for the characterization of different functionalities carried by nanoparticles as well as their interaction with living systems was outlined

Cedervall T., Lynch I., Lindman S., Berggard T., Thulin E., Nilsson H., Dawson K. A. and Linse S. (2007) Understanding the nanoparticle-protein corona using methods to quantify exchange rates and affinities of proteins for nanoparticles. *Proc. Natl. Acad. Sci U. S. A* **104**, 2050-2055.

Abstract: Due to their small size, nanoparticles have distinct properties compared with the bulk form of the same materials. These properties are rapidly revolutionizing many areas of medicine and technology. Despite the remarkable speed of development of nanoscience, relatively little is known about the interaction of nanoscale objects with living systems. In a biological fluid, proteins associate with nanoparticles, and the amount and presentation of the proteins on the surface of the particles leads to an in vivo response. Proteins compete for the nanoparticle "surface," leading to a protein "corona" that largely

defines the biological identity of the particle. Thus, knowledge of rates, affinities, and stoichiometries of protein association with, and dissociation from, nanoparticles is important for understanding the nature of the particle surface seen by the functional machinery of cells. Here we develop approaches to study these parameters and apply them to plasma and simple model systems, albumin and fibrinogen. A series of copolymer nanoparticles are used with variation of size and composition (hydrophobicity). We show that isothermal titration calorimetry is suitable for studying the affinity and stoichiometry of protein binding to nanoparticles. We determine the rates of protein association and dissociation using surface plasmon resonance technology with nanoparticles that are thiol-linked to gold, and through size exclusion chromatography of protein-nanoparticle mixtures. This method is less perturbing than centrifugation, and is developed into a systematic methodology to isolate nanoparticle-associated proteins. The kinetic and equilibrium binding properties depend on protein identity as well as particle surface characteristics and size.

Chen Y., Wang F. and Benson H. A. (2008) Effect of formulation factors on incorporation of the hydrophilic peptide dalargin into PLGA and mPEG-PLGA nanoparticles. *Biopolymers* **90**, 644-650.
Abstract: The objective of this study was to examine formulation factors that influence the incorporation of the hydrophilic peptide dalargin into poly(D, L-lactic-co-glycolic acid) (PLGA) and methoxy-polyethylene glycol (mPEG)-PLGA nanoparticles. In particular, the effect of ionic additives and nanoparticle method of preparation on the incorporation of dalargin and resultant nanoparticle properties was investigated. Biodegradable nanoparticles were prepared from mPEG-PLGA and PLGA by both solvent evaporation and solvent diffusion methods with inclusion of ionic additives of dextran sulphate (DS), sulfobutyl ether-beta-cyclodextrin (SB-CD), or sodium dodecyl sulfate (SDS). The resultant nanoparticles were analyzed for their mean particle size and size distribution, zeta-potential, peptide loading, yield, and morphology. The inclusion of ionic additives in the nanoparticle formulation significantly influenced dalargin entrapment efficiency (EE). For example, with the PLGA/SDS formulation EE increased from 13.3% to 91.2% and from 4.1% to 68.6% with the solvent diffusion and evaporation methods, respectively. The inclusion of ionic surfactant SDS has also led to the formation of smaller size of nanoparticles. Isothermal titration microcalorimetry revealed a strong interaction between dalargin and DS, medium level interaction with SDS, and weak interaction with SB-CD. The results of this study suggest that a strong ionic interaction between peptides and additives may lead to enhanced peptide incorporation but also increased particle size. Intermediate ionic interaction, especially when it is associated with the formation of reversed micelles in a hydrophobic polymer solution, could be used to enhance the incorporation of hydrophilic peptides in PLGA and mPEG-PLGA nanoparticles

Contarino M. R., Sergi M., Harrington A. E., Lazareck A., Xu J., and Chaiken I. (2006) Modular, self-assembling peptide linkers for stable and regenerable carbon nanotube biosensor interfaces. *J Mol Recognit* **19**, 363-371.

Abstract: As part of an effort to develop nanoelectronic sensors for biological targets, we tested the potential to incorporate coiled coils as metallized, self-assembling, site-specific molecular linkers on carbon nanotubes (CNTs). Based on a previously conceived modular anchor-probe approach, a system was designed in which hydrophobic residues (valines and leucines) form the interface between the two helical peptide components. Charged residues (glutamates and arginines) on the borders of the hydrophobic interface increase peptide solubility, and provide stability and specificity for anchor-probe assembly. Two histidine residues oriented on the exposed hydrophilic exterior of each peptide were included as chelating sites for metal ions such as cobalt. Cysteines were incorporated at the peptide termini for oriented, thiol-mediated coupling to surface plasmon resonance (SPR) biosensor surfaces, gold nanoparticles or CNT substrates. The two peptides were produced by solid phase peptide synthesis using Fmoc chemistry: an acidic 42-residue peptide E42C, and its counterpart in the heterodimer, a basic 39-residue peptide R39C. The ability of E42C and R39C to bind cobalt was demonstrated by immobilized metal affinity chromatography and isothermal titration calorimetry. SPR biosensor kinetic analysis of dimer assembly revealed apparent sub-nanomolar affinities in buffers with and without 1 mM CoCl₂ using two different reference surfaces. For device-oriented CNT immobilization, R39C was covalently anchored to CNT tips via a C-terminal cysteine residue. Scanning electron microscopy was used to visualize the assembly of probe peptide (E42C) N-terminally labeled with 15 nm gold nanoparticles, when added to the R39C-CNT surface. The results obtained open the way to develop CNT tip-directed recognition surfaces, using

recombinant and chemically synthesized chimeras containing binding epitopes fused to the E42C sequence domain.

Dai X. H., Dong C. M. and Yan D. (2008) Supramolecular and biomimetic polypseudorotaxane/glycopolymer biohybrids: synthesis, glucose-surfaced nanoparticles, and recognition with lectin. *J Phys. Chem B* **112**, 3644-3652.

Abstract: A new class of supramolecular and biomimetic glycopolymer/poly(epsilon-caprolactone)-based polypseudorotaxane/glycopolymer triblock copolymers (poly(D-gluconamidoethyl methacrylate)-PPR-poly(D-gluconamidoethyl methacrylate), PGAMA-PPR-PGAMA), exhibiting controlled molecular weights and low polydispersities, was synthesized by the combination of ring-opening polymerization of epsilon-caprolactone, supramolecular inclusion reaction, and direct atom transfer radical polymerization (ATRP) of unprotected D-gluconamidoethyl methacrylate (GAMA) glycomonomer. The PPR macroinitiator for ATRP was prepared by the inclusion complexation of biodegradable poly(epsilon-caprolactone) (PCL) with alpha-cyclodextrin (alpha-CD), in which the crystalline PCL segments were included into the hydrophobic alpha-CD cavities and their crystallization was completely suppressed. Moreover, the self-assembled aggregates from these triblock copolymers have a hydrophilic glycopolymer shell and an oligosaccharide threaded polypseudorotaxane core, which changed from spherical micelles to vesicles with the decreasing weight fraction of glycopolymer segments. Furthermore, it was demonstrated that these triblock copolymers had specific biomolecular recognition with concanavalin A (Con A) in comparison with bovine serum albumin (BSA). To the best of our knowledge, this is the first report that describes the synthesis of supramolecular and biomimetic polypseudorotaxane/glycopolymer biohybrids and the fabrication of glucose-shelled and oligosaccharide-threaded polypseudorotaxane-cored aggregates. This hopefully provides a platform for targeted drug delivery and for studying the biomolecular recognition between sugar and lectin

De M., You C. C., Srivastava S. and Rotello V. M. (2007) Biomimetic interactions of proteins with functionalized nanoparticles: a thermodynamic study. *J Am. Chem Soc.* **129**, 10747-10753.

Abstract: Gold nanoparticles (NPs) functionalized with L-amino acid-terminated monolayers provide an effective platform for the recognition of protein surfaces. Isothermal titration calorimetry (ITC) was used to quantify the binding thermodynamics of these functional NPs with alpha-chymotrypsin (ChT), histone, and cytochrome c (CytC). The enthalpy and entropy changes for the complex formation depend upon the nanoparticle structure and the surface characteristics of the proteins, e.g., distributions of charged and hydrophobic residues on the surface. Enthalpy-entropy compensation studies on these NP-protein systems indicate an excellent linear correlation between ΔH and $T\Delta S$ with a slope (α) of 1.07 and an intercept ($T\Delta S_0$) of 35.2 kJ mol⁻¹. This behavior is closer to those of native protein-protein systems ($\alpha = 0.92$ and $T\Delta S_0 = 41.1$ kJ mol⁻¹) than other protein-ligand and synthetic host-guest systems.

de la Fuente J. M., Eaton P., Barrientos A. G., Menendez M., and Penades S. (2005) Thermodynamic evidence for Ca²⁺-mediated self-aggregation of Lewis X gold glyconanoparticles. A model for cell adhesion via carbohydrate-carbohydrate interaction. *J Am Chem Soc* **127**, 6192-6197.

Abstract: Thermodynamic evidence for the selective Ca²⁺-mediated self-aggregation via carbohydrate-carbohydrate interactions of gold glyconanoparticles functionalized with the disaccharides lactose (lacto-Au) and maltose (malto-Au), or the biologically relevant trisaccharide Lewis X (Le(X)-Au), was obtained by isothermal titration calorimetry. The aggregation process was also directly visualized by atomic force microscopy. It was shown in the case of the trisaccharide Lewis X that the Ca²⁺-mediated aggregation is a slow process that takes place with a decrease in enthalpy of 160 +/- 30 kcal mol⁻¹, while the heat evolved in the case of lactose and maltose glyconanoparticles was very low and thermal equilibrium was quickly achieved. Measurements in the presence of Mg²⁺ and Na⁺ cations confirm the selectivity for Ca²⁺ of Le(X)-Au glyconanoparticles. The relevance of this result to cell-cell adhesion process mediated by carbohydrate-carbohydrate interactions is discussed.

Huang D., Korolev N., Eom K. D., Tam J. P. and Nordenskiold L. (2008) Design and biophysical characterization of novel polycationic epsilon-peptides for DNA compaction and delivery. *Biomacromolecules.* **9**, 321-330.

Abstract: Design and solid-phase synthesis of novel and chemically defined linear and branched -oligo(1-lysines) (denoted -K_n, where n is the number of lysine residues) and their alpha-substituted homologues (epsilon-(R)K₁₀, epsilon-(Y)K₁₀, epsilon-(L)K₁₀, epsilon-(YR)K₁₀, and epsilon-(LYR)K₁₀) for DNA

compaction and delivery are reported. The ability to condense viral (T2 and T4) and plasmid DNA as well as the size of -peptide DNA complexes under different conditions was investigated with static and dynamic light scattering, isothermal titration calorimetry, and fluorescence microscopy. Nanoparticle diameters varied from 100 to 150 and 375 to 550 nm for plasmid and T4 DNA peptide complexes, respectively. Smaller sizes were observed for oligo(L-lysines) compared to alpha-poly(L-lysine). The linear -oligo-lysines are less toxic and epsilon-(LYR)K10 showed higher transfection efficiency in HeLa cells than corresponding controls. The results also demonstrate that with a branched design having pendent groups of short alpha-oligopeptides, improved transfection can be achieved. This study supports the hypothesis that available alpha-oligo-lysine derived systems would potentially have more favorable delivery properties if they are based instead on epsilon-oligo(L-lysines). The flexible design and unambiguous synthesis that enables variation of pendent groups holds promise for optimization of such -peptides to achieve improved DNA compaction and delivery

Lindman S., Lynch I., Thulin E., Nilsson H., Dawson K. A. and Linse S. (2007) Systematic investigation of the thermodynamics of HSA adsorption to N-iso-propylacrylamide/N-tert-butylacrylamide copolymer nanoparticles. Effects of particle size and hydrophobicity. *Nano. Lett* **7**, 914-920.

Abstract: Nanoparticles in biological fluids almost invariably become coated with proteins that may confer nanomedical and nanotoxicological effects. Understanding these effects requires quantitative measurements using simple systems. Adsorption of HSA to copolymer nanoparticles of varying hydrophobicity and curvature was studied using ITC, yielding stoichiometry, affinity, and enthalpy changes upon binding. The hydrophobicity was controlled via the co-monomer ratio, N-iso-propylacrylamide/N-tert-butylacrylamide. The most hydrophobic particles become fully covered with a single layer of protein, except at high curvature.

Linse S., Cabaleiro-Lago C., Xue W. F., Lynch I., Lindman S., Thulin E., Radford S. E. and Dawson K. A. (2007) Nucleation of protein fibrillation by nanoparticles. *Proc. Natl. Acad. Sci U. S. A* **104**, 8691-8696.

Abstract: Nanoparticles present enormous surface areas and are found to enhance the rate of protein fibrillation by decreasing the lag time for nucleation. Protein fibrillation is involved in many human diseases, including Alzheimer's, Creutzfeldt-Jacob disease, and dialysis-related amyloidosis. Fibril formation occurs by nucleation-dependent kinetics, wherein formation of a critical nucleus is the key rate-determining step, after which fibrillation proceeds rapidly. We show that nanoparticles (copolymer particles, cerium oxide particles, quantum dots, and carbon nanotubes) enhance the probability of appearance of a critical nucleus for nucleation of protein fibrils from human beta(2)-microglobulin. The observed shorter lag (nucleation) phase depends on the amount and nature of particle surface. There is an exchange of protein between solution and nanoparticle surface, and beta(2)-microglobulin forms multiple layers on the particle surface, providing a locally increased protein concentration promoting oligomer formation. This and the shortened lag phase suggest a mechanism involving surface-assisted nucleation that may increase the risk for toxic cluster and amyloid formation. It also opens the door to new routes for the controlled self-assembly of proteins and peptides into novel nanomaterials.

Meister A., Drescher S., Mey I., Wahab M., Graf G., Garamus V. M., Hause G., Mogel H. J., Janshoff A., Dobner B. and Blume A. (2008) Helical nanofibers of self-assembled bipolar phospholipids as template for gold nanoparticles. *J Phys. Chem B* **112**, 4506-4511.

Abstract: Bipolar phospholipids (bolalipids) represent an exciting class of amphiphilic molecules as they self-assemble in water to distinct structures of nanoscopic dimensions. Reported here are structural details of helical nanofibers, composed of achiral, symmetrical single-chain bolalipids with phosphocholine headgroups. These nanofibers are used as template for the fixation of gold nanoparticles (AuNPs) without prior functionalization. This realization of a metal array on bolalipid nanofibers is one of the rare examples of one-dimensional AuNP arrangements in solution. The loading and the heat of binding of AuNPs are determined applying transmission electron microscopy and isothermal titration calorimetry

Nizri G., Lagerge S., Kamyshny A., Major D. T. and Magdassi S. (2008) Polymer-surfactant interactions: binding mechanism of sodium dodecyl sulfate to poly(diallyldimethylammonium chloride). *J Colloid Interface Sci* **320**, 74-81.

Abstract: The binding mechanism of poly(diallyldimethylammonium chloride), PDAC, and sodium dodecyl sulfate, SDS, has been comprehensively studied by combining binding isotherms data with

microcalorimetry, zeta potential, and conductivity measurements, as well as ab initio quantum mechanical calculations. The obtained results demonstrate that surfactant-polymer interaction is governed by both electrostatic and hydrophobic interactions, and is cooperative in the presence of salt. This binding results in the formation of nanoparticles, which are positively or negatively charged depending on the molar ratio of surfactant to PDAC monomeric units. From microcalorimetry data it was concluded that the exothermic character of the interaction diminishes with the increase in the surfactant/polymer ratio as well as with an increase in electrolyte concentration

Quadir M. A., Radowski M. R., Kratz F., Licha K., Hauff P. and Haag R. (2008) Dendritic multishell architectures for drug and dye transport. *J Control Release (epublication)*.

Abstract: Here we present the efficiency and versatility of newly developed core-multishell nanoparticles (CMS NPs), to encapsulate and transport the antitumor drugs doxorubicin hydrochloride (Dox), methotrexate (Mtx) and sodium ibandronate (Ibn) as well as dye molecules, i.e., a tetrasulfonated indotricarbocyanine (ITCC) and Nile red. Structurally, the CMS NPs are composed of hyperbranched poly(ethylene imine) core functionalized by alkyl diacids connected to monomethyl poly(ethylene glycol). In order to evaluate their transport in aqueous media in vitro, we have used and compared SEC, UV, ITC, and NMR techniques. We observed that the CMS NPs were able to spontaneously encapsulate and transport Dox, Mtx and Nile red in both organic and aqueous media as determined by SEC and UV-VIS spectroscopy. For the VIS transparent Ibn Isothermal Titration Calorimetric (ITC) experiments show an exothermic interaction with the CMS NPs. The enthalpic stabilization (ΔH) upon encapsulation was in the order of approximately 7 kcal/mol which indicates stable interaction between Ibn and nanoparticles. A T(1) inversion recovery NMR experiment was carried out for (^{31}P) and (^1H) nuclei of Ibn and an increment of spin-lattice relaxation time for respective nuclei was observed upon encapsulation. CMS NPs were also found to encapsulate ITCC dye with stoichiometry of 6-8 molecules/nanocarrier. For in vivo imaging studies the dye loaded CMS NPs were injected to F9 teratocarcinoma bearing mice and a strong contrast was observed in the tumor tissues compared to free dye after 6 h of administration

Rautaray D., Mandal S., and Sastry M. (2005) Synthesis of hydroxyapatite crystals using amino acid-capped gold nanoparticles as a scaffold. *Langmuir* **21**, 5185-5191.

Abstract: Inorganic composites are of special interest for biomedical applications such as in dental and bone implants wherein the ability to modulate the morphology and size of the inorganic crystals is important. One interesting possibility to control the size of inorganic crystals is to grow them on nanoparticles. We report here the use of surface-modified gold nanoparticles as templates for the growth of hydroxyapatite crystals. Crystal growth is promoted by a monolayer of aspartic acid bound to the surface of the gold nanoparticles; the carboxylate ions in aspartic acid are excellent binding sites for Ca^{2+} ions. Isothermal titration calorimetry studies of Ca^{2+} ion binding with aspartic acid-capped gold nanoparticles indicates that the process is entropically driven and that screening of the negative charge by the metal ions leads to their aggregation. The aggregates of gold nanoparticles are believed to be responsible for assembly of the platelike hydroxyapatite crystals into quasi-spherical superstructures. Control experiments using uncapped gold nanoparticles and pure aspartic acid indicate that the amino acid bound to the nanogold surface plays a key role in inducing and directing hydroxyapatite crystal growth.

Srinivasachari S., Liu Y., Prevette L. E. and Reineke T. M. (2007) Effects of trehalose click polymer length on pDNA complex stability and delivery efficacy. *Biomaterials* **28**, 2885-2898.

Abstract: Cationic polymers are currently being studied as non-viral vectors to deliver therapeutic DNA into cells. In this study, a series of trehalose-based glycopolymers containing four secondary amines in the repeat unit were synthesized via the 'click reaction' [degrees of polymerization ($n(w)$)=35, 53, 75, or 100] to elucidate how the polymer length affects the bioactivity. The four structures bound and charge-neutralized pDNA with similar affinity that was independent of the length, as determined through gel electrophoresis, heparin competitive displacement, and isothermal titration calorimetric assays. Dynamic light scattering measurements revealed that the polyplexes formed with the longer polymers ($n(w)$ =53, 75, or 100) inhibited flocculation in media containing serum, whereas the polyplexes formed with the shorter polymer ($n(w)$ =35) aggregated rapidly. Similar results were observed via transmission electron microscopy studies, where the nanoparticles formed with the polymers having longer degrees of polymerization showed discrete particles in media containing 10% serum. Transfection experiments revealed that the polymers exhibited low cytotoxicity at low N/P ratios and could facilitate high cellular uptake and gene expression in

HeLa and H9c2(2-1) cells, and the results were dependent on the degrees of polymerization (longer polymers yielded higher transfection and toxicity).

Stolnik S., Heald C. R., Garnett M. G., Illum L., and Davis S. S. (2005) Differences in the adsorption behaviour of poly(ethylene oxide) copolymers onto model polystyrene nanoparticles assessed by isothermal titration microcalorimetry correspond to the biological differences. *J Drug Target* **13**, 449-458.

Abstract: The adsorption behaviour of a tetrafunctional copolymer of poly(ethylene oxide)-poly(propylene oxide) ethylene diamine (commercially available as Poloxamine 908) and a diblock copolymer of poly(lactic acid)-poly(ethylene oxide) (PLA/PEG 2:5) onto a model colloidal drug carrier (156 nm sized polystyrene latex) is described. The adsorption isotherm, hydrodynamic thickness of the adsorbed layers and enthalpy of the adsorption were assessed. The close similarity in the conformation of the poly(ethylene oxide) (PEO) chains (molecular weight 5000 Da) in the adsorbed layers of these two copolymers was demonstrated by combining the adsorption data with the adsorbed layer thickness data. In contrast, the results from isothermal titration microcalorimetry indicated a distinct difference in the interaction of the copolymers with the polystyrene colloid surface. Poloxamine 908 adsorption to polystyrene nanoparticles is dominated by an endothermic heat effect, whereas, PLA/PEG 2:5 adsorption is entirely an exothermic process. This difference in adsorption behaviour could provide an explanation for differences in the biodistribution of Poloxamine 908 and PLA/PEG 2:5 coated polystyrene nanoparticles observed in previous studies. A comparison with the interaction enthalpy for several other PEO-containing copolymers onto the same polystyrene colloid was made. The results demonstrate the importance of the nature of the anchoring moiety on the interaction of the adsorbing copolymer with the colloid surface. An endothermic contribution is found when an adsorbing molecule contains a poly(propylene oxide) (PPO) moiety (e.g. Poloxamine 908), whilst the adsorption is exothermic (i.e. enthalpy driven) for PEO copolymers with polylactide (PLA/PEG 2:5) or alkyl moieties.

You C. C., Agasti S. S. and Rotello V. M. (2008) Isomeric control of protein recognition with amino acid- and dipeptide-functionalized gold nanoparticles. *Chemistry* **14**, 143-150.

Abstract: Amino acid and dipeptide-functionalized gold nanoparticles (NPs) possessing L/D-leucine and/or L/D-phenylalanine residues have been constructed in order to target the surfaces of alpha-chymotrypsin (ChT) and cytochrome c (CytC). Isothermal titration calorimetry (ITC) was conducted to evaluate the binding thermodynamics and selectivity of these NP-protein interactions. The chirality of the NP end-groups substantially affects the resultant complex stability, with up to 20-fold differences seen between particles of identical hydrophobicity, demonstrating that structural information from the ligands can be used to control protein recognition