

DSC XX - Polymer Studies

Abraham G. A., Gallardo A., San Roman J., Fernandez-Mayoralas A., Zurita M., and Vaquero J. (2003) Polymeric matrices based on graft copolymers of PCL onto acrylic backbones for releasing antitumoral drugs. *J Biomed Mater Res* **64A**, 638-647.

Abstract: Graft copolymers of poly(epsilon-caprolactone) (PCL) on poly(dimethylacrylamide) (PDMAm), poly(methylmethacrylate) (PMMA), or on copolymers of poly(DMAm-co-MMA) have been synthesized and characterized by ¹H NMR spectroscopy, differential scanning calorimetry (DSC), and size exclusion chromatography (SEC). These partially biodegradable copolymer matrices have been proposed as drug delivery systems for the release of low-molecular-weight glycosides. Octyl-N-acetyl-6-O-[2,2-bis(hydroxymethyl)-3-hydroxypropyl]-alpha-D-glucos amide, a synthetic carbohydrate able to inhibit the proliferation of human malignant glioma cells in culture and transplanted glioma in rats was selected as drug model. The in vitro aqueous behavior of four drug-loaded and unloaded graft copolymers of different MMA: DMAm and PCL ratios has been analyzed performing swelling, degradation, and drug release experiments. An intimate dependence of the aqueous behavior with the composition has been found. The higher was the DMAm content, the higher was the hydrophilicity of the synthesized systems as well as the swelling, degradation, and drug release rate. In vivo experiments in pigs demonstrated the very good tolerance of drug-loaded implanted polymeric discs, and that >95% of the charged drug is released after 2 months' implantation.

Abraham G. A., Marcos-Fernandez A., and Roman J. S. (2006) Bioresorbable poly(ester-ether urethane)s from L-lysine diisocyanate and triblock copolymers with different hydrophilic character. *J Biomed Mater Res A* **76**, 729-736.

Abstract: Bioresorbable linear poly(ester-ether urethane)s with different hydrophilic character were synthesized from block copolymers of poly(epsilon-caprolactone)-poly(ethylene oxide)-poly(epsilon-caprolactone) (PCL-PEO-PCL) as macrodiols, and L-lysine diisocyanate (LDI). A series of PCL-PEO-PCL triblock copolymers with different PEO and PCL chain length was obtained by reacting PEO with epsilon-caprolactone. Polyurethanes were synthesized by reacting the triblock copolymers with LDI in solution using stannous 2-ethylhexanoate as catalyst. The prepared triblock copolymers and polyurethanes were fully characterized by proton nuclear magnetic resonance spectroscopy, size exclusion chromatography, differential scanning calorimetry, and wide-angle X-ray diffraction. Water uptake, hydrolytic stability, and tensile properties of polyurethanes with different composition were evaluated and discussed in terms of the chain length and molecular weight of the polymers and its block components. Water uptake seems to depend on the ethylene oxide unit content of the polyurethane regardless of the triblock structure. Mechanical properties of the synthesized polymers were strongly affected by the molecular weight achieved during polymerization. The use of triblock macrodiols with different hydrophilicity allowed the preparation of a series of polyurethanes having a broad range of properties.

Almeida N. L., Oliveira C. L., Torriani I. L., and Loh W. (2004) Calorimetric and structural investigation of the interaction of lysozyme and bovine serum albumin with poly(ethylene oxide) and its copolymers. *Colloids Surf B Biointerfaces* **38**, 67-76.

Abstract: This work reports investigations aiming at verifying the occurrence of specific interactions between lysozyme or bovine serum albumin (BSA) and poly(ethylene oxide) and its copolymers with poly(propylene oxide). Thermal stability of these proteins, followed by means of high sensitivity DSC, was found to be mostly unaffected by the presence of these polymers. Chromatographic experiments (reverse-phase HPLC and size exclusion chromatography) did not reveal any sign of specific interaction for these mixtures, either. Isothermal titration calorimetry revealed an increase in enthalpy for the mixtures, represented by a positive enthalpy of transfer for these proteins from buffer to polymer solutions. Moreover, SAXS analyses confirmed that at ambient temperatures these polymers do not affect lysozyme structure. In summary, no evidence is found to support earlier suggestions that some kind of complex could be formed between these proteins and poly(ethylene oxide) or its copolymers, but the present results suggest the occurrence of entropically driven hydrophobic effects.

Anderson B. C., Cox S. M., Ambardekar A. V., and Mallapragada S. K. (2002) The effect of salts on the micellization temperature of aqueous poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide) solutions and the dissolution rate and water diffusion coefficient in their corresponding gels. *J Pharm Sci* **91**, 180-188.

Abstract: Studies were performed to examine the effect of ionic salts on phase transitions, dissolution rates, and diffusion coefficients of water in gels of poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide) with polymer concentrations ranging from 22 to 32% w/w and salt concentrations ranging from 0 to 1.5% w/w. Salts tested include Na₃PO₄, Na₂SO₄, Na₂HPO₄, NaH₂PO₄, NaCH₃CO₂, NaCl, and KI. Micellization transition temperatures were obtained using differential scanning calorimetry. The dissolution rates were obtained by measurement of the surface erosion rates, and diffusion coefficients were obtained by using a method to analyze the intrusion of water into the aqueous gels. It was found that salts had no effect on the dissolution rate of the polymer gels into deionized water. However, when the salt concentration in the aqueous dissolution media was adjusted to match the concentration in the gels, the dissolution rate of the polymer gel decreased with increasing salt concentration. The salts also had a profound effect on the critical micellization temperature (CMT) and the diffusion coefficient of water within the gel. The diffusion coefficient and CMT decreased in the presence of salts. The magnitude of these effects was comparable to their placement on the Hofmeister, or lyotropic series for salts. The effects of polymer and salt concentrations on the CMT were quantified, and a single correlation was proposed to predict the micellization temperatures for a wide range of salt and polymer concentrations.

Andronova N. and Albertsson A. C. (2006) Resilient bioresorbable copolymers based on trimethylene carbonate, L-lactide, and 1,5-dioxepan-2-one. *Biomacromolecules* **7**, 1489-1495.

Abstract: The new combinations of monomers presented in this work were evaluated in order to create an elastic material for potential application in soft tissue engineering. Thermoplastic elastomers (TPE) of trimethylene carbonate (TMC) with L-lactide (LLA) and 1,5-dioxepan-2-one (DXO) have been synthesized using a cyclic five-membered tin alkoxide initiator. The block copolymers were designed in such a way that poly(trimethylene carbonate-co-1,5-dioxepan-2-one) formed an amorphous middle block and the poly(L-lactide) (PLLA) formed semicrystalline terminal blocks. The amorphous middle block consisted of relatively randomly distributed TMC and DXO monomer units, and the defined block structure of the PLLA terminal segments was confirmed by ¹³C NMR. The properties of the TMC-DXO-LLA copolymers were compared with those of triblock copolymers based either on LLA-TMC or on LLA-DXO. Differential scanning calorimetry and dynamic mechanical analysis data confirmed the micro-phase separation in the copolymers. The mechanical properties of the copolymers were evaluated using tensile testing and cycling loading. All of the copolymers synthesized showed a highly elastic behavior. The properties of copolymers could be tailored by altering the proportions of the different monomers.

Armstrong J. K., Chowdhry B. Z., Snowden M. J., Dong J., and Leharne S. A. (2001) The effect of pH and concentration upon aggregation transitions in aqueous solutions of poloxamine T701. *Int J Pharm* **229**, 57-66.

Abstract: Thermally induced aggregation transitions have been investigated for aqueous solutions of the poloxamine block copolymer T701-(OE(4)OP(13))(2)NCH(2)CH(2)N(OP(13)OE(4))(2)-using differential scanning calorimetry. The calorimetric signals obtained were fitted to a mass action model description of aggregation using a previously reported analytical procedure (Patterson et al., *Langmuir* **13** (1997) 2219). The presence of a central ethylene diamine moiety in the molecular structure renders the T701 molecule basic; this was confirmed and measured by acid/base titration. Basicity is shown to have an important impact upon aggregation. At low pH (2.5), the poloxamine exists in its protonated form and the bulk solution proton concentration is sufficient to suppress de-protonation, aggregation-as a consequence-is shifted to a higher temperature range. Any increase in pH reduces the temperature range over which aggregation occurs. The derived experimental calorimetric parameters, obtained from model fitting procedures, can be used to compute the fraction of poloxamine existing in an aggregated form, at any particular temperature. The data sets obtained were interpolated to show that at human body temperature (310.6 K) the fraction of poloxamine found in its aggregated form is zero at a pH of 2.5. However at a pH of 6.8, the percentage aggregation increases to about 85%. These aggregation characteristics of T701 have important implications for the design of drug delivery systems, which incorporate poloxamines.

Arvisenet G., Le Bail P., Voilley A., and Cayot N. (2002) Influence of physicochemical interactions between amylose and aroma compounds on the retention of aroma in food-like matrices. *J Agric Food Chem* **50**, 7088-7093.

Abstract: In food matrices, where starch is often used as a gelling or texturing agent, the occurrence of amylose-aroma complexes and their effect on the release of aroma compounds are difficult to determine. Indeed, thick or gelled systems are known to reduce the diffusion rate of flavor molecules, resulting in an increase of retention. Moreover, interactions between aroma compounds and matrix components might increase the retention of aroma compounds. The complexing behavior of three aroma compounds with amylose was studied by DSC and X-ray diffraction to determine the relative importance of these two factors. Their interaction properties were different: two of them formed complexes, and the third did not. These aroma compounds were added in food matrices containing different starches that induced different textures. Their retention was studied by static headspace analysis. The retention of aroma compounds appeared to depend on the amylose/amylopectin ratio of starch, both from the formation of complexes and by a viscosity effect.

Artzner F., Geiger S., Olivier A., Allais C., Finet S. and Agnely F. (2007) Interactions between poloxamers in aqueous solutions: micellization and gelation studied by differential scanning calorimetry, small angle X-ray scattering, and rheology. *Langmuir* **23**, 5085-5092.

Abstract: Poloxamers F88 (EO97PO39EO97) and P85 (EO27PO39EO27) are triblock copolymers of ethylene oxide (EO) and propylene oxide (PO), which have the same hydrophobic PO block. We studied aqueous solutions of these two copolymers by the conjoint use of differential scanning calorimetry (DSC), rheology, and small-angle X-ray scattering (SAXS). The results showed that the temperature-induced micellization of aqueous solutions of F88 and P85 was a progressive process followed by gelation for sufficiently concentrated samples. Gelation was due to the ordered packing of micelles under a hexagonal compact (HC) structure for P85 and a body-centered cubic (BCC) phase for F88. Importantly, the phase diagram of F88/P85 mixtures in water was elucidated and showed the destabilization of the HC phase upon addition of small amounts of F88.

Babin J., Rodriguez-Hernandez J., Lecommandoux S., Klok H. A., and Achard M. F. (2005) Self-assembled nanostructures from peptide-synthetic hybrid block copolymers: complex, stimuli-responsive rod-coil architectures. *Faraday Discuss* **128**, 179-192.

Abstract: The synthesis, solution and solid state self-assembly properties of a series of polyisoprene-b-poly(epsilon-benzoyloxycarbonyl-L-lysine) PI-b-PZLys and polyisoprene-b-poly(L-lysine) PI-b-PLys block copolymers have been examined. The formation of stimuli-responsive micelles in water has been studied as a function of pH and ionic strength using static and dynamic light scattering, UV-circular dichroism and transmission electron microscopy. The observed change in the micelles dimensions has been directly attributed to the conformational transition in the secondary structure of polypeptide chains. In bulk, these rod-coil copolymers form self-assembled structures that have been characterized using DSC, DMA, WAXS and SAXS techniques. Hexagonal in lamellar (HL) and more interestingly hexagonal in hexagonal (HH) morphologies have been evidenced as a function of the chemical composition.

Barbera J., Puig L., Romero P., Serrano J. L., and Sierra T. (2005) Supramolecular helical mesomorphic polymers. Chiral induction through H-bonding. *J Am Chem Soc* **127**, 458-464.

Abstract: The work described here concerns a challenge of general interest in supramolecular chemistry: the achievement of chiral helical organizations with controlled structures. This work provides a strategy to obtain supramolecular polymers in which a chiral helical conformation has been induced by a noncovalent association, that is, through hydrogen bonding. Polycatenar 2,4,6-triarylamino-1,3,5-triazines, which organize into columnar mesophases and are susceptible to H-bonding interactions, were chosen as a starting point to build up the chiral supramolecular structure. The stacking of these mesogens has been forced to wind in a helical way by means of H-bond association with (R)-3-methyladipic acid, within the mesophase. The optically active columnar organization has been studied in depth by optical microscopy, differential scanning calorimetry (DSC), X-ray diffraction, and circular dichroism. Formation of stable complexes between the triazine units and (R)-3-methyladipic acid has also been investigated by means of NMR diffusion-ordered spectroscopy (DOSY) experiments in chloroform.

Barbuzzi T., Giuffrida M., Impallomeni G., Carnazza S., Ferreri A., Guglielmino S. P., and Ballistreri A. (2004) Microbial synthesis of poly(3-hydroxyalkanoates) by *Pseudomonas aeruginosa* from fatty acids: identification of higher monomer units and structural characterization. *Biomacromolecules* **5**, 2469-2478. **Abstract:** *Pseudomonas aeruginosa* ATCC 27853 accumulated poly(3-hydroxyalkanoates) (PHAs) after growth on saturated fatty acids with an odd number of carbon atoms. No nutrient limitation was required to induce PHA synthesis, although better yields were obtained when the medium was magnesium deprived. A comparative study was carried out between PHAs obtained from C-odd and those from C-even carbon sources. Repeating units identification was performed by gas chromatography (GC) and capillary liquid chromatography-electrospray mass spectrometry (LC-ESI MS) of methanolized samples. When C-odd n-alkanoic acids from nonanoic to pentadecanoic were used the lowest hydroxyalkanoate unit found was 3-hydroxyvalerate and the highest 3-hydroxypentadecanoate, whereas when C-even acids from octanoic to eicosanoic were used these were 3-hydroxycaproate and 3-hydroxyeicosanoate, respectively. Weight average molecular weights were in the range 187 000-596 000. DSC traces showed T_m and ΔH_m which varied from 43 to 58 degrees C and from 5.9 to 24.8 J/g, with the PHAs generated from C-odd carbon sources having lower values. ESI MS of partially pyrolyzed samples allowed the identification of oligomers up to heptamers, and statistical analysis of the ions intensity in the mass spectra showed that these PHAs are random copolyesters.

Bellot M. and Bouteiller L. (2008) Thermodynamic Description of Bis-urea Self-Assembly: Competition between Two Supramolecular Polymers. *Langmuir (epublication)*. **Abstract:** Supramolecular polymers are chains of small molecules held together through reversible noncovalent interactions. In general, a given monomer self-assembles into a single type of supramolecular polymer. However, in a few cases, two different self-assembled structures can coexist; this yields interesting responsive systems. To improve the understanding of these systems, we report an association model describing the self-assembly of a supramolecular polymer into two competing forms. The parameters controlling the system were measured by high sensitivity differential scanning calorimetry and isothermal titration calorimetry in the case of a hydrogen-bonded bis-urea supramolecular polymer solution in toluene. The model enables us to compute the proportion and length of all components in the system at any temperature and concentration. The results of these calculations are in agreement with the experimental phase diagram and with independent viscosity measurements

Berggren J. and Alderborn G. (2003) Effect of polymer content and molecular weight on the morphology and heat- and moisture-induced transformations of spray-dried composite particles of amorphous lactose and poly(vinylpyrrolidone). *Pharm Res* **20**, 1039-1046. **Abstract:** **PURPOSE:** The aim was to investigate the influence of polymer content and molecular weight on the morphology and heat- and moisture-induced transformations, as indicators of stability, of spray-dried composite particles of amorphous lactose and poly(vinylpyrrolidone) (PVP). **METHODS:** Amorphous lactose and composite particles of amorphous lactose with different contents and molecular weights of PVP were prepared by spray drying. The nanostructure of the particles was analyzed by x-ray powder diffractometry, the morphology by light microscopy and SEM, the glass transition temperatures (T_g), crystallization temperatures (T_c), heats of crystallization and melting temperatures by differential scanning calorimetry, and moisture-induced crystallizations gravimetrically and by microcalorimetry. **RESULTS:** All the types of particles prepared were amorphous. The T_g was unchanged or only marginally increased as a result of the inclusion of PVP. However, crystallization temperature, time to moisture-induced crystallization, and particle morphology were affected by both content and molecular weight of PVP. **CONCLUSIONS:** Increased content and molecular weight of PVP may have the potential to increase the physical stability of amorphous lactose. However, T_g seems not to be a relevant indicator for the stability of this type of amorphous composite materials.

Blennow A., Bay-Smidt A. M., Olsen C. E., and Moller B. L. (2000) The distribution of covalently bound phosphate in the starch granule in relation to starch crystallinity. *Int J Biol Macromol* **27**, 211-218. **Abstract:** Five selected starches with a 60-fold span in their content of monoesterified starch phosphate were investigated with respect to distribution of glucose 6-phosphate and glucose 3-phosphate residues, amylopectin chain length distributions and gelatinisation properties. The distribution of starch phosphate in the starch granules was determined by preparation of Nageli dextrans followed by quantitative ^{31}P -nuclear magnetic resonance spectroscopy. Total starch phosphate content was positively correlated to the unit chain

lengths of the amylopectin as well as to the chain lengths of the corresponding Nageli dextrans. The major part (68-92%) of the total starch phosphate content was partitioned to the hydrolysed (amorphous) parts. Starch-bound glucose 6-phosphate per milligram of starch was 2-fold enriched in the amorphous parts, whereas phosphate groups bound at the 3-position were more evenly distributed. The gelatinisation temperatures of the native starches as determined by differential scanning calorimetry were positively correlated ($R(2)=0.75$) to starch phosphate content, while crystallinity (gelatinisation enthalpy) and crystal heterogeneity (endotherm peak width) showed no correlations to starch phosphate content. The relations between starch molecular structure, architecture and functional properties are discussed.

Bogracheva T. Y., Wang Y. L., Wang T. L., and Hedley C. L. (2002) Structural studies of starches with different water contents. *Biopolymers* **64**, 268-281.

Abstract: The proportion of double helices in starches from a series of pea [rb, rug4-b, rug3-a, and lam-c mutants, and the wild type (WT) parental line], potato and maize (normal and low amylose), and wheat (normal) lines, ranged from about 30-50% on a dry weight basis. In relatively dry starch powders, only about half of the double helices were in crystalline order, this proportion being higher for A-type than for B-type starches. Using starch from WT pea as an example, it was found that increasing water content results in an increase in total crystallinity. When the water content was raised to a level similar to that in excess water, the proportion of crystallinity was close to the proportion of double helices (DH). Measuring crystallinity in starches with a high water content is difficult using traditional methods such as x-ray diffraction. A method was developed, therefore, for determining starch structural characteristics in excess water by measuring the enthalpy of gelatinization transition in quasi-equilibrium differential scanning calorimetry (DSC) experiments. It is suggested that $DH\% = \Delta H(sp)/\Delta H(DH) \times 100\%$, where $\Delta H(sp)$ and $\Delta H(DH)$ represent the specific enthalpies of gelatinisation transition, $\Delta H(sp)$ being measured as J/g dry starch weight and $\Delta H(DH)$ as J/g DH, in starch. Studies on potato and maize starches in excess water and in 0.6M KCl showed, respectively, that $\Delta H(DH)$ was 36.3 and 35.6 J/g for B-type polymorphs and 33.0 and 35.0 J/g for A-type polymorphs. For C-type starches, such as those from pea, intermediate values of $\Delta H(DH)$, related to the proportions A-/B-polymorphs, should be used. The type of crystallinity in starch can be determined by the shift in peak temperature for thermograms in excess water and in excess 0.6M KCl. For B-polymorphs this shift was found to be approximately 2-3 degrees C and for A-polymorphs approximately 7-12 degrees C. The ratio between ordered areas with both A- and B-polymorphs can be determined from the enthalpies of disruption of each area. These enthalpies can be obtained by deconvolution of bimodal thermograms produced by C-type starches in excess 0.6M KCl. This methodical approach can be applied to all starches that give a sharp gelatinisation thermogram in excess water. Using a range of methods, including DSC, it was found that starch granules from the mutant peas are constructed in a similar way to those from the WT, with B-polymorphs in the centre and A-polymorphs at the periphery of all granules. The proportion of A/B-polymorphs, however, differed between the mutants. It was found that in addition to increasing the total crystallinity, increasing the water content within the granules also resulted in an increase in the proportion of B-polymorphs.

Breitenbach A., Li Y. X., and Kissel T. (2000) Branched biodegradable polyesters for parenteral drug delivery systems. *J Control Release* **64**, 167-178.

Abstract: Continuous, 'infusion-like' drug release profiles from biodegradable parenteral delivery systems are difficult to achieve for proteins and other hydrophilic macromolecular drugs with commonly used linear polyesters from lactic acid (PLA) and its random copolymers with glycolic acid (PLG). Drug release rates can be modified either by increasing the hydrophilicity of polyesters or by manipulating the polymer architecture to adjust polymer degradation rates and thus drug release. Therefore, we investigated different branching concepts for biodegradable polyesters of PLA and PLG. For one four- and eight-arm poly(ethylene oxide)s (PEO) were grafted with shorter polyester chains leading to star-branched structures. Secondly we obtained comb-like polyesters using both charged and uncharged dextrans or poly(vinyl alcohol)s (PVA) as hydrophilic backbones. The star-shaped and brush-like grafted polymers were intensively characterized by methods, such as NMR, IR, SEC-SLS, DSC and viscosity measurements. Tailor-made properties make these novel biodegradable polyesters promising candidates for parenteral protein delivery systems. While the star-branched polyesters have shown some interesting properties with respect to their degradation behavior, retaining the PEO blocks longer than ABA triblock copolymers, their release properties need further optimization. Brush-like branched polyesters on the other hand seem to

possess both degradation and release properties meriting further investigations for parenteral protein delivery systems.

Breitenbach A., Mohr D., and Kissel T. (2000) Biodegradable semi-crystalline comb polyesters influence the microsphere production by means of a supercritical fluid extraction technique (ASES). *J Control Release* **63**, 53-68.

Abstract: The aerosol solvent extraction system (ASES) is a method based on solvent extraction using supercritical carbon dioxide for the preparation of microspheres. The ASES technology seems to be strongly affected by physico-chemical properties of biodegradable polymers, leading to incomplete or unsuccessful microsphere formation. The number of suitable polymers for ASES, such as poly(L-lactide) (L-PLA) and poly(beta-hydroxy-butyric acid) (PHB) is rather limited for unknown reasons. Therefore linear and novel branched polyesters were synthesized and subjected to the ASES process to explore the function property relationship. The properties of these polymers as well as of the ASES products were characterized by NMR spectroscopy, differential scanning calorimetry, light scattering, wide-angle X-ray scattering and scanning electron microscopy. It appears that high degrees of polymer crystallinity are the key factor for successful microsphere formation using the ASES process. Under the conditions investigated two types of polymers were especially suitable: semi-crystalline comb polyesters as well as comb polyesters in which crystallinity could be induced. These novel polymers are of particular interest for the ASES encapsulation technology since they combine beneficial properties both controlling drug release due to their three-dimensional architecture and faster biodegradability with sufficient mechanical stability to allow particle formation using supercritical carbon dioxide.

Brissault B., Kichler A., Leborgne C., Jarroux N., Cheradame H. and Guis C. (2007) Amphiphilic Poly[(propylene glycol)-block-(2-methyl-2-oxazoline)] Copolymers for Gene Transfer in Skeletal Muscle. *ChemMedChem*. **2**, 1202-1207.

Abstract: Amphiphilic triblock copolymers such as poly(ethylene glycol-b-propylene glycol-b-ethylene glycol) PE6400 (PEG(13)-PPG(30)-PEG(13)) have been recently shown to promote gene transfer in muscle. Herein we investigated the effect of a chemical change of the PEG moiety on the transfection activity of these compounds. We synthesized new amphiphilic copolymers in which the PEG end blocks are replaced by more hydrophilic poly(2-methyl-2-oxazoline) (PMeOxz) chains of various lengths. The resulting triblock PMeOxz-PPG-PMeOxz compounds were characterized by NMR, SEC, TGA, and DSC techniques and assayed for in vivo muscle gene transfer. The results confirm both the block structure and the monomer unit composition (DP(PG)/DP(PMeOxz)) of the new PPG(34)-PMeOxz(41) and PPG(34)-PMeOxz(21) triblock copolymers. Furthermore, in vivo experiments show that these copolymers are able to significantly increase DNA transfection efficiency, despite the fact that their chemical nature and hydrophilic character are different from the poloxamers. Overall, these results show that the capacity to enhance DNA transfection in skeletal muscle is not restricted to PEG-PPG-PEG arrangements.

Buleon A., Gallant D. J., Bouchet B., Mouille G., D'Hulst C., Kossmann J., and Ball S. (1997) Starches from A to C. *Chlamydomonas reinhardtii* as a model microbial system to investigate the biosynthesis of the plant amylopectin crystal. *Plant Physiol* **115**, 949-957.

Abstract: Wide-angle powder x-ray diffraction analysis was carried out on starch extracted from wild-type and mutant *Chlamydomonas reinhardtii* cells. Strains containing no defective starch synthases as well as mutants carrying a disrupted granule-bound starch synthase structural gene displayed the A type of diffraction pattern with a high degree of crystallinity. Mutants carrying a defect for the major soluble starch synthase (SSS), SSS II, were characterized by a switch to the B type of diffraction pattern with very low crystallinity. Mutant strains carrying SSS I as the only glucan elongation enzyme regained some of their crystallinity but switched to the C type of diffraction pattern. Differential scanning calorimetry analysis correlated tightly with the x-ray diffraction results. Together with the electron microscopy analyses, these results establish *C. reinhardtii* as a microbial model system displaying all aspects of cereal starch synthesis and structure. We further show that SSS II is the major enzyme involved in the synthesis of crystalline structures in starch and demonstrate that SSS I alone builds a new type of amylopectin structure.

Cai Q., Bei J., and Wang S. (2000) Synthesis and degradation of a tri-component copolymer derived from glycolide, L-lactide, and epsilon-caprolactone. *J Biomater Sci Polym Ed* **11**, 273-288.

Abstract: A series of tri-component copolymers was synthesized by ring opening copolymerization of

cyclic lactones, i.e. glycolide, L-lactide, and caprolactone, using stannous octoate as a catalyst. Various techniques, including FT-IR, ¹H NMR, DSC, X-ray diffraction, tensile strength, and contact angle measurements, were used to elucidate structural characteristics, thermal behavior, mechanical properties, and hydrophilicity of the resulting copolymers. Data showed that the properties of these copolymers could be modulated by adjusting the composition of the copolymers. The DSC and X-ray analysis demonstrated amorphous structures for most of the PGLC copolyesters. The degradation behavior of these PGLC copolymers had been studied in vitro, i.e. in 0.10 M pH 7.4 phosphate buffer solution (PBS). The degradation was monitored by intrinsic viscosity and weight loss measurements. SEM and GPC were also used to monitor the morphology and molecular weight change during degradation. The PGLC copolymers were shown to have variable degradation rates, and most of them could disappear within a few months due to their amorphous structure and low glass transition temperature.

Cai Q. X., Zhu K. J., Chen D., and Gao L. P. (2003) Synthesis, characterization and in vitro release of 5-aminosalicylic acid and 5-acetyl aminosalicylic acid of polyanhydride--P(CBFAS). *Eur J Pharm Biopharm* **55**, 203-208.

Abstract: A novel polyanhydride, poly[(5-carboxybutyl formamide)-2-acetyl salicylic anhydride] (P(CBFAS)), with 5-aminosalicylic acid (5-ASA) incorporated into the polymer backbone was synthesized and characterized by infrared, (1)H-nuclear magnetic resonance, differential scanning calorimetry, vapor pressure osmometry, etc. The polyanhydride was subjected to degradation and simultaneously released 5-ASA and its derivative 5-acetyl aminosalicylic acid (5-acetyl ASA) in vitro under various conditions. The factors influencing the release profiles of 5-ASA and 5-acetyl ASA, including polymer molecular weights, pH value, enzyme and rat gastrointestinal contents, were examined. The results showed that the release rate of 5-ASA and 5-acetyl ASA increases with increasing pH value and with decreasing molecular weights. In PBS (pH 8.0, 37 degrees C) total ASA released was 8.0% for P(CBFAS)(1) (Mn 10770) in 13 h, but only 1.1 and 2.6% at pH 2.0 and 6.5, respectively. Enzymes including pepsin and trypsin, as well as rat gastric and jejunum contents had little effect on the release rate of 5-ASA and 5-acetyl ASA at pH 2.0 and 6.5 (less than 4% in 13 h). However, the release rate of 5-ASA and 5-acetyl ASA was much fast in PBS(pH 8.0) containing 5% of cecal contents, the total ASA released was 13.6% for the polymer in 13 h. Considering the high drug loading of the polymer (50.2% of 5-ASA moieties in the backbones) and the degradation characters, it is possible to reach high local concentration of 5-ASA in the colon site via oral administration. Therefore, P(CBFAS) may be potentially useful in the colon specific delivery of 5-ASA.

Calandrelli L., De Rosa G., Errico M. E., La Rotonda M. I., Laurienzo P., Malinconico M., Oliva A., and Quaglia F. (2002) Novel graft PLLA-based copolymers: potential of their application to particle technology. *J Biomed Mater Res* **62**, 244-253.

Abstract: This study describes the synthesis of novel biodegradable graft copolymers based on a backbone of poly (L-lactic acid) (PLLA) on which short blocks of polyacrylamide (PAcr) were grafted. Preliminary results of their potential in the field of controlled-release technologies also have been reported. The copolymers have been synthesized through the radical polymerization of acrylamide initiated by a peroxide in the presence of PLLA. Two different methodologies of synthesis, namely, in solution and in emulsion, have been tested. The structure of the copolymers was studied by (1)H-NMR and infrared spectroscopy and by differential scanning calorimetry (DSC) and cytotoxicity tests were conducted to assess their biocompatibility. The copolymers were used to prepare particles by the emulsion-solvent evaporation technique. The shapes and dimensions of the particles were dependent on the polymer type and concentration used. The surfaces of the particles were modified by the presence of polyacrylamide residues, as demonstrated by zeta-potential measurements. The release behavior of the particles was assessed by encapsulating rhodamine B as the model compound. The release was faster for the particles prepared by the grafted polymer as a consequence of its increased hydrophilicity. Based on these novel biomaterials, preliminary results suggest a potential of the particles for peroral or parenteral drug delivery.

Caminade A. M., Laurent R., and Majoral J. P. (2005) Characterization of dendrimers. *Adv Drug Deliv Rev* **57**, 2130-2146.

Abstract: Dendrimers pertain both to the molecular chemistry world for their step by step controlled syntheses, and to the polymer world because of their repetitive structure made of monomers; thus they benefit from analytical techniques from both worlds. This review is a survey of the main analytical techniques used for the characterization of the chemical composition, the morphology, the shape, and the

homogeneity of dendrimers. It includes NMR, IR, Raman, UV-Visible, fluorescence, circular dichroism, X-ray diffraction, mass spectrometry, SAXS, SANS, Laser Light Scattering, microscopy, SEC, EPR, electrochemistry, electrophoresis, intrinsic viscosity, DSC, and dielectric spectroscopy.

Campbell P., Ma S., Yeom B., McKellop H., Schmalzried T. P., and Amstutz H. C. (1995) Isolation of predominantly submicron-sized UHMWPE wear particles from periprosthetic tissues. *J Biomed Mater Res* **29**, 127-131.

Abstract: A method of tissue digestion using sodium hydroxide was applied to the isolation and recovery of ultra-high-molecular-weight polyethylene (UHMWPE) particles from tissues around failed total hip replacements. Density gradient ultracentrifugation of the digested tissues was performed to separate the UHMWPE from cell debris and other particulates. Fourier transform infrared spectroscopy and differential scanning calorimetry (DSC) verified that the recovered particles were UHMWPE. When viewed by scanning electron microscopy, individual particles were clearly observed and were either rounded or elongated. The majority were submicron in size. The application of this method to the study of particles from periprosthetic tissues may elucidate aspects of biomaterial particle size and shape that are important to the biologic response to, and clinical outcome of, total joint replacement.

Canciello M., Maglio G., Nese G. and Palumbo R. (2007) Poly(epsilon-caprolactone)-poly(oxyethylene) multiblock copolymers bearing along the chain regularly spaced pendant amino groups. *Macromol. Biosci.* **7**, 491-499.

Abstract: Poly(epsilon-caprolactone) (PCL) macromers ($M(n) = 1.7-3.8$ kDa) which contain one Z-protected -NH₂ group per chain were synthesized by ring-opening polymerization of epsilon-caprolactone in the presence of Sn(oct)₂ using as initiator a diamine prepared by condensation of N-Boc-1,6-hexanediamine and N(alpha)-Boc-N(epsilon)-Z-L-Lysine. The coupling of these macromers with -COCl end-capped poly(oxyethylene) (PEO), $M(n) = 1.0$ kDa, afforded amphiphilic multiblock poly(ether ester)s (PEEs) which have, along the chain, regularly spaced pendant protected amino groups. Deprotection, accomplished without chain degradation, yielded -NH₂ groups available for further reactions. The molecular structure of macromers and PEEs was investigated by ¹H NMR and SEC. DSC and WAXS analyses showed that macromers and copolymers were semicrystalline and their $T(m)$ increased with increase in the molecular weight of PCL segments. The inherent viscosity values (0.25-0.30 dL x g⁻¹), together with SEC analysis results, indicated moderate polymerization degrees.

Cappello J., Crissman J. W., Crissman M., Ferrari F. A., Textor G., Wallis O., Whitley J. R., Zhou X., Burman D., Aukerman L., and Stedronsky E. R. (1998) In-situ self-assembling protein polymer gel systems for administration, delivery, and release of drugs. *J Control Release* **53**, 105-117.

Abstract: Sequential block copolymers consisting of tandem repetition of amino acids have been constructed and genetically produced based on the natural repeating structures of silk and elastin protein. Combinations of silklike and elastinlike amino acid sequence blocks in a high molecular weight protein polymer are used to confer properties similar to those observed with hard block and soft block segmented polyurethanes. A certain subset of these silk-elastinlike protein compositions, termed ProLastins, will undergo an irreversible solution to gel transition in physiological, aqueous solution. The transition occurs over time and can be controlled by temperature, solution conditions, and additives which either prevent or promote hydrogen bond-mediated chain crystallization. The process involves no covalent crosslinking. Characterization of the gelling properties of various ProLastin compositions and their ability to release compounds which are incorporated directly into the gels are presented.

Carey D. H. (2000) The surface stability of polymers with adsorbed fibronectin. *J Biomed Mater Res* **49**, 12-16.

Abstract: Linear low-density polyethylene (LLDPE), polypropylene (PP), polystyrene (PS), and polyethylene-co-ethacrylic acid (PE-EAA, 17.5% acid content) films were treated with an aqueous solution of fibronectin. Advancing contact angles of water (straight theta(a)) were used to monitor the change in the surface wettability of these films. With the exception of PE-EAA, all of the samples showed an increase in their wettability by water, indicating that the protein had adsorbed to the polymer surface. The stability of these protein-modified films against a buffered aqueous solution and against air under ambient conditions was monitored over time. The surface wettability of these protein-modified polymers, with the exception of PS, remained unchanged after heating against the buffer solution. In air, however, straight theta(a)

increased over a period of 2 months. In addition, the effect of organic solvent extraction on the surface stability of these protein-modified films was investigated. Unmodified samples of LLDPE, PS, and PP were subjected to Soxhlet extraction to remove impurities and low-molecular-weight oligomers prior to film preparation and subsequent treatment with fibronectin. These samples were left in air under ambient conditions for 2 months. There was no difference in the magnitude of the change in straight theta(α) for the protein-modified, extracted LLDPE film compared to the protein-modified, nonextracted polymer film. A slight decrease in the rate of thermal reconstruction was observed for the protein-modified extracted PS film compared to the protein-modified nonextracted sample, and a slight increase in the rate of thermal reconstruction was observed for the protein-modified extracted PP film compared to the protein-modified nonextracted sample. Copyright 2000 John Wiley & Sons, Inc.

Cascone M. G., Barbani N., Cristallini C., Giusti P., Ciardelli G., and Lazzeri L. (2001) Bioartificial polymeric materials based on polysaccharides. *J Biomater Sci Polym Ed* **12**, 267-281.

Abstract: Bioartificial polymeric materials, based on blends of polysaccharides with synthetic polymers such as poly(vinyl alcohol) (PVA) and poly(acrylic acid) (PAA), were prepared as films or hydrogels. The physico-chemical, mechanical, and biological properties of these materials were investigated by different techniques such as differential scanning calorimetry, dynamic mechanical thermal analysis, scanning electron microscopy, and in vitro release tests, with the aim of evaluating the miscibility of the polymer blends and to establish their potential applications. The results indicate that while dextran is perfectly miscible with PAA, dextran/PVA, chitosan/PVA, starch/PVA, and gellan/PVA blends behave mainly as two-phase systems, although interactions can occur between the components. Cross-linked starch/PVA films could be employed as dialysis membranes: they showed transport properties comparable to, and in some cases better than, those of currently used commercial membranes. Hydrogels based on dextran/PVA and chitosan/PVA blends could find applications as delivery systems. They appeared able to release physiological amounts of human growth hormone, offering the possibility to modulate the release of the drug by varying the content of the biological component.

Ceccorulli G., Scandola M., Kumar A., Kalra B., and Gross R. A. (2005) Cocrystallization of random copolymers of omega-pentadecalactone and epsilon-caprolactone synthesized by lipase catalysis. *Biomacromolecules* **6**, 902-907.

Abstract: Random copolymers were prepared by *Candida antarctica* lipase B (Novozyme-435) catalyzed copolymerization of omega-pentadecalactone (PDL) with epsilon-caprolactone (CL). Over the whole composition range PDL-CL copolymers are highly crystalline (melting enthalpy by differential scanning calorimetry, above 100 J/g; crystallinity degree by wide-angle X-ray scattering, WAXS, 60-70%). The copolymers melt at temperatures that linearly decrease with composition from that of poly(omega-pentadecalactone) (PPDL; 97 degrees C) to that of poly(epsilon-caprolactone) (PCL; 59 degrees C). The WAXS profiles of PCL and PPDL homopolymers are very similar, except for the presence in PPDL of the (001) reflection at $2\theta = 4.58$ degrees that corresponds to a 19.3 angstroms periodicity in the chain direction. In PDL-CL copolymers the intensity of this reflection decreases with increasing content of CL units and vanishes at 50 mol % CL, as a result of randomization of the ester group alignment and loss of chain periodicity. PDL-CL copolymers crystallize in a lattice that gradually changes from that of one homopolymer to that of the other, owing to comonomer isomorphous substitution. Cocrystallization of comonomer units is also shown by a random PDL-CL copolymer obtained in a polymerization/transesterification reaction catalyzed by *C. antarctica* lipase B (Novozyme-435) starting from preformed PCL and PDL monomer.

Chaubal M. V., Su G., Spicer E., Dang W., Branham K. E., English J. P., and Zhao Z. (2003) In vitro and in vivo degradation studies of a novel linear copolymer of lactide and ethylphosphate. *J Biomater Sci Polym Ed* **14**, 45-61.

Abstract: Poly(lactide-co-ethylphosphate)s, a new class of linear phosphorus-containing copolymers made by chain-extending low-molecular-weight polylactide prepolymers with ethyl dichlorophosphate, were investigated for their in vitro and in vivo degradation mechanism and kinetics. Microspheres made from poly(lactide-co-ethylphosphate) were studied under both accelerated and normal in vitro degradation conditions. Gel permeation chromatography (GPC), ¹H- and ³¹P-NMR, weight loss measurements, and differential scanning calorimetry (DSC) techniques were used to characterize the change of molecular weight (M(w)), chemical composition, and glass transition temperature (T(g)) of the degrading polymers.

The results indicated that the copolymers degraded in a two-stage fashion, with cleavage of the phosphate-lactide linkages contributing mostly to the initial more rapid degradation phase and cleavage of the lactide-lactide bonds being responsible for the slower latter stage degradation. The decrease in the copolymer $M(w)$ was accompanied by a continuous mass loss. Results from the accelerated degradation studies confirmed that the copolymers degraded into various monomers of the copolymers, which were non-toxic and biocompatible. A two-stage hydrolysis pathway was thus proposed to explain the degradation behavior of the copolymers. In vivo degradation studies performed in mice demonstrated a good in vitro and in vivo correlation for the degradation rates. In vivo clearance of the polymer was faster and without any lag phase. These copolymers are potentially advantageous for drug delivery and other biomedical applications where rapid clearance of the polymer carrier and repeated dosing capability are essential to the success of the treatment.

Chen B., Baumeister U., Pelzl G., Das M. K., Zeng X., Ungar G., and Tschierske C. (2005) Carbohydrate rod conjugates: ternary rod-coil molecules forming complex liquid crystal structures. *J Am Chem Soc* **127**, 16578-16591.

Abstract: T-shaped polyphilic triblock molecules, consisting of a rodlike p-terphenyl unit, a hydrophilic and flexible laterally attached oligo(oxyethylene) chain terminated by an 1-acylamino-1-deoxy-D-sorbitol unit, and two end-attached lipophilic alkyl chains, have been synthesized by palladium-catalyzed cross-coupling reactions as the key steps. The thermotropic liquid crystalline behavior of these compounds was investigated by polarized light microscopy, differential scanning calorimetry (DSC), and X-ray scattering. We investigated the mode of self-organization as a function of the length and position of the lateral polar chain and the length of the terminal alkyl chains. Depending on the size of the polar and lipophilic segments, a series of unusual liquid crystalline phases was detected. In three of these phases, the space is divided into three distinct periodic subspaces. In addition to a hexagonal channeled layer phase (ChL(hex)) consisting of layers that are penetrated by polar columns, there are also two honeycomb-like network structures formed by square (Col(squ)/p4mm) or pentagonal cylinders (Col(squ)/p4gm). The cylinder walls consist of the terphenyl units fused by columns of alkyl chains, and the interior contains the polar side chains. In addition, a hexagonal columnar phase was observed in which the polar columns are organized in a continuum of terphenyls and alkyl chains with an organization of the terphenyl cores tangentially around the columns with the long axis perpendicular to the columns. For one compound, a reversal of birefringence was observed, which is explained by a reorientation of the terphenyl cores. The addition of protic solvents induces lamellar phases.

Cheng M., Deng J., Yang F., Gong Y., Zhao N., and Zhang X. (2003) Study on physical properties and nerve cell affinity of composite films from chitosan and gelatin solutions. *Biomaterials* **24**, 2871-2880.

Abstract: A series of chitosan-gelatin composite films was prepared by varying the ratio of constituents. FT-IR and X-ray analysis showed good compatibility between these two biopolymers. Differential scanning calorimetry (DSC) analysis indicated that the water take-up of chitosan film increased when blended with gelatin. Composite film exhibited a lower Young's modulus and a higher percentage of elongation-at-break compared with chitosan film, especially in wet state. All composite films were hydrophilic materials with water contact angles ranging from 55 degrees to 65 degrees. The results obtained from ELISA indicated the adsorption amount of fibronectin on composite films was much higher than on chitosan film. PC12 cells culture was used to evaluate the nerve cell affinity of materials. The cells cultured on the composite film with 60wt% gelatin differentiated more rapidly and extended longer neurites than on chitosan film. The results suggest that the soft and elastic complex of chitosan and gelatin, which has better nerve cell affinity compared to chitosan, is a promising candidate biomaterial for nerve regeneration.

Chia H. H., Yang Y. Y., Chung T. S., Ng S., and Heller J. (2001) Auto-catalyzed poly(ortho ester) microspheres: a study of their erosion and drug release mechanism. *J Control Release* **75**, 11-25.

Abstract: A study has been carried out to investigate the degradation and protein release mechanisms of BSA-loaded microspheres made with auto-catalyzed poly(ortho esters) (POEs) of varying diol composition and molecular weights. Due to the instability of the POE/dichloromethane primary emulsion, microspheres made using the W/O/W double emulsion solvent extraction/evaporation method showed a multivesicular internal structure. An O/W single emulsion process yielded dense POE microspheres. Using electron scanning microscopy, the microspheres were observed to erode throughout their matrices with increasing

internal pore sizes and a steady loss of mass. However, despite a substantial weight loss of almost 80% after an in vitro period of 129 days, the molecular weight of the polymer remained relatively unchanged with loss averaging about 18 and 32% for low- and high-molecular-weight POEs, respectively. Such constancy in molecular weight was similarly reflected in the glass transition temperature of the degrading microspheres. The differences in both the molecular weight loss and polydispersity index changes depended largely on the molecular weight of the polymer. For protein release of POE microspheres, an induction period followed by BSA release for a period of 3 to 10 days was observed. The lag time depended on the hydrophilicity and the molecular weight of the polymer as well as the morphology of the microspheres. Protein release was incomplete, possibly due to the slow degradation of the POE polymers, protein aggregation and protein degradation.

Chiotelli E., Pilosio G., and Le Meste M. (2002) Effect of sodium chloride on the gelatinization of starch: a multimeasurement study. *Biopolymers* **63**, 41-58.

Abstract: The effect of sodium chloride on the gelatinization and rheological properties of wheat and potato starches has been studied using differential scanning calorimetry, dynamic mechanical thermal analysis, and electron spin resonance techniques. All samples contained 60% water (w/w wet starch basis) and the salt content ranged from 0 to 16% (g/100 g starch-water). The presence of salt affected the onset (T(o)), peak (T(p)), and end (T(e)) temperatures of gelatinization, gelatinization enthalpy (ΔH), storage modulus (G'), and rotational mobility coefficient (D(rot)), and the effect differed by salt concentration. ¹H-NMR was used in parallel in order to elucidate how salts affect the properties of water in starch suspensions and in aqueous salt solutions according to their position on the Hofmeister series classification. The obtained results suggest that the mechanism of starch gelatinization in salt solutions can be attributed to the effect of solute on water properties and direct polymer-solute interactions. These two effects conflict with one another and result in complex effect patterns depending on the concentration of the salts.

Cho K. Y., Moon J. Y., Lee Y. W., Lee K. G., Yeo J. H., Kweon H. Y., Kim K. H., and Cho C. S. (2003) Preparation of self-assembled silk sericin nanoparticles. *Int J Biol Macromol* **32**, 36-42.

Abstract: Silk sericin (SS) possessing moisture-retaining property was reacted with activated poly(ethylene glycol) (PEG) to obtain self-assembled SS nanoparticles. The aliphatic and aromatic hydroxyl groups of serine and tyrosine residues as the reaction sites in SS were clarified by amino acid analysis and ¹H NMR spectroscopy, respectively. From IR and circular dichroism (CD) measurements, introduction of PEG into SS induced the conformational change from random coil to beta-sheet. DSC thermogram of sericin-PEG conjugate suggests that mutual miscibility between PEG and SS chains was poor. Nanoparticles of sericin-PEG conjugate with sizes measured by dynamic light scattering ranging about 200-400 nm in diameter, were prepared by the diafiltration method. Shape of sericin-PEG conjugate nanoparticles observed by scanning and transmission electron microscopes was spherical. The results suggest that sericin-PEG conjugates are self-associated to form spherical nanoparticles through hydrophobic interaction.

Choosakoonkriang S., Lobo B. A., Koe G. S., Koe J. G., and Middaugh C. R. (2003) Biophysical characterization of PEI/DNA complexes. *J Pharm Sci* **92**, 1710-1722.

Abstract: The main goal of this study was to determine the effects of polyethylenimine (PEI) molecular weight and structure (750 kDa, 25 kDa, 2 kDa branched, and 25 kDa linear PEI) and the nitrogen/phosphate (N/P) molar ratio on the physical properties and transfection efficiencies of PEI/DNA complexes. Fourier transform infrared spectroscopy revealed that DNA remained in the B conformation when complexed to all PEIs. Unique alterations in the circular dichroism spectra of DNA were observed in the presence of each PEI, whereas differential scanning calorimetry measurements showed that all PEIs examined destabilized supercoiled DNA at N/P < 3/1, but not at higher ratios. Isothermal titration calorimetry revealed the existence of protonation changes at low ionic strength due to possible shifts in pK(a) of the ionizable groups of PEI during complex formation. Twenty-five kilodalton branched and 25 kDa linear PEI complexes showed the highest transfection efficiencies at an N/P ratio of 6:1 in COS-7 and CHO-K1 cells, respectively. These investigations have detected alterations in the physical and colloidal properties of the complexes that were sensitive to polymer structure, molecular weight, and polymer/DNA ratio, but these properties did not directly correlate with their transfection efficiencies. To further probe any possible relationship between these parameters and activity, a more refined biophysical analysis of any

subpopulations in these samples that may differ in transfection activity is suggested, although the existence of such species remains unknown.

Cilurzo F., Minghetti P., Selmin F., Casiraghi A., and Montanari L. (2003) Polymethacrylate salts as new low-swellable mucoadhesive materials. *J Control Release* **88**, 43-53.

Abstract: The sodium and potassium salts of the methacrylic copolymers Eudragit L100 and Eudragit S100 were prepared with the aim to develop new low-swellable mucoadhesive materials intended for the preparation of buccal dosage forms. The physico-chemical characterization of the copolymers and the corresponding sodium and potassium salts was performed by using Fourier-transform infrared (FT-IR) spectroscopy and thermal analysis. When ionization occurred, the carboxylic acid group absorption band (1730 cm⁻¹) was replaced by another characteristic band at 1560 cm⁻¹. After salification the T_g of the two polymers shifted towards higher values and it was not significantly influenced by the contraion nature. The intrinsic dissolution rate at infinite rotation speed ($7.354 < G(\infty) < 9.196$) was about 6- to 7-fold higher than that of a low nominal viscosity hydroxypropylmethylcelluloses (HPMC). Moreover, the Eudragit salts did not show an evident swelling layer and their dissolution is governed by erosion. The adhesion properties of these materials, evaluated by texture analysis, overlapped with those of Carbopol 934P. On the basis of the in vivo bioadhesion test, the prepared methacrylic salts can be considered interesting for the preparation of both buccal tablets and patches with good patient compliance due to their low swelling properties.

Dahmani M., Ramzi M., Rochas C., and Guenet J. M. (2003) Thermoreversible gelation in aqueous binary solvents of chemically modified agarose. *Int J Biol Macromol* **31**, 147-153.

Abstract: The thermoreversible gelation of chemically modified agarose has been studied in aqueous binary solvents (dimethyl sulfoxide and a series of formamide) by differential calorimetry, mechanical testing, and small-angle neutron scattering. The temperature-composition phase diagrams have been established. It is concluded that gelation is promoted by the formation of ternary complexes modified agarose/water/cosolvent, wherein the cosolvent mediates the interaction between chains through the formation of electrostatic interactions.

Dai Y., Lambert L., Yuan Z. and Keller J. (2008) Characterisation of polyhydroxyalkanoate copolymers with controllable four-monomer composition. *J Biotechnol.* **134**, 137-145.

Abstract: Polyhydroxyalkanoate (PHA) copolymers comprising the four monomers 3-hydroxybutyrate (3HB), 3-hydroxyvalerate (3HV), 3-hydroxy-2-methylvalerate (3HMB) and 3-hydroxy-2-methylbutyrate (3HMB) were generated using the recently discovered *DeFluviicoccus vanus*-related glycogen accumulating organisms (DvGAOs) under anaerobic conditions without applying any nutrient limitations. The composition could be manipulated in a defined range by modifying the ratio of propionate and acetate provided in the feed stream. The PHAs produced were characterised as random copolymers (from propionate alone) or a mixture of random copolymers (from mixture of propionate and acetate) through microstructure analysis using ¹³C NMR spectroscopy. The sequence distribution of all eight comonomer pairs in the carbonyl region of 3HB and 3HV was identified and assigned with confidence utilising two-dimensional heteronuclear multiple bond coherence (HMBC) spectroscopy. Weight average molecular weights were in the range 390-560 kg/mol. Differential scanning calorimetry (DSC) traces showed that the melting temperature (T_m) varied between 70 and 161 degrees C and glass transition temperature (T_g) ranged from -8 to 0 degrees C. The incorporation of considerable amounts of 3HMB and 3HMB monomer units introduced additional "defects" into the PHBV copolymer structure and hence greatly lowered the crystallinity. The data indicate the potential of these four-monomer PHAs to be employed for practical applications, considering their favourable properties and the cost-effective production process using a mixed culture and simple carbon sources

Deschamps A. A., van Apeldoorn A. A., Hayen H., de Bruijn J. D., Karst U., Grijpma D. W., and Feijen J. (2004) In vivo and in vitro degradation of poly(ether ester) block copolymers based on poly(ethylene glycol) and poly(butylene terephthalate). *Biomaterials* **25**, 247-258.

Abstract: Two in vivo degradation studies were performed on segmented poly(ether ester)s based on polyethylene glycol (PEG) and poly(butylene terephthalate) (PBT) (PEOT/PBT). In a first series of experiments, the in vivo degradation of melt-pressed discs of different copolymer compositions were followed up for 24 weeks after subcutaneous implantation in rats. The second series of experiments aimed

to simulate long-term in vivo degradation. For this, PEOT/PBT samples were pre-degraded in phosphate buffer saline (PBS) at 100 degrees C and subsequently implanted. In both series, explanted materials were characterized by intrinsic viscosity measurements, mass loss, proton nuclear magnetic resonance spectroscopy (¹H-NMR) and differential scanning calorimetry (DSC). In both studies the copolymer with the higher PEO content degraded the fastest, although all materials degraded relatively slowly. To determine the nature of the degradation products formed during hydrolysis of the copolymers, 1000 PEOT71PBT29 (a copolymer based on PEG with a molecular weight of 1000 g/mol and 71 wt% of PEO-containing soft segments) was degraded in vitro at 100 degrees C in phosphate buffer saline (PBS) during 14 days. The degradation products present in PBS were analyzed by ¹H-NMR and high performance liquid chromatography/mass spectroscopy (HPLC/MS). These degradation products consisted of a fraction with high contents of PEO that was soluble in PBS and a PEOT/PBT fraction that was insoluble at room temperature. From the different in vitro and in vivo degradation experiments performed, it can be concluded that PEOT/PBT degradation is a slow process and generates insoluble polymeric residues with high PBT contents.

Ding Y., Ye X. and Zhang G. (2008) Can coil-to-globule transition of a single chain be treated as a phase transition? *J Phys. Chem B* **112**, 8496-8498.

Abstract: The effects of the concentration (C) and heating rate on the collapse and association of poly(N-isopropylacrylamide) chains in water have been investigated by use of ultrasensitive differential scanning calorimetry. In the dilute solutions, both the phase transition temperature (T_p) and enthalpy change (ΔH) increase with the heating rate but decrease with concentration. By extrapolation to zero heating rate and zero concentration, T_p and ΔH for coil-to-globule transition of a single chain in thermodynamic equilibrium can be obtained. In semidilute solutions, both T_p and ΔH increase with the heating rate but slightly vary with the concentration. T_p and ΔH for pure interchain association in equilibrium are obtained by extrapolation to zero heating rate. Our experiments reveal that only intrachain contraction occurs when the concentration is infinitely close to zero. When the concentration is above the overlap concentration (C*), only interchain association exists. In the range 0 < C < C*, both intrachain contraction and interchain association coexist

Dizman B., Elasri M. O., and Mathias L. J. (2005) Synthesis, characterization, and antibacterial activities of novel methacrylate polymers containing norfloxacin. *Biomacromolecules* **6**, 514-520.

Abstract: A novel methacrylate monomer containing a quinolone moiety was synthesized and homopolymerized in N,N-dimethylformamide (DMF) by using azobisisobutyronitrile (AIBN) as an initiator. The new monomer was copolymerized with poly(ethylene glycol) methyl ether methacrylate (MPEGMA) in DMF using the same initiator. The monomer, homopolymer, and copolymer were characterized by elemental analysis, thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), size exclusion chromatography (SEC), FTIR, (¹³C NMR, and (¹H NMR. The antibacterial activities of the monomer as well as polymers were investigated against *Staphylococcus aureus* and *Escherichia coli*, which are representative of Gram-positive and Gram-negative bacteria, respectively. All compounds showed excellent antibacterial activities against these two types of bacteria. The antibacterial activities were determined using the shaking flask method, where 25 mg/mL concentrations of each compound were tested against 10(5) CFU/mL bacteria solutions. The number of viable bacteria was calculated by using the spread plate method, where 100 microL of the incubated antibacterial agent in bacteria solutions were spread on agar plates and the number of viable bacteria was counted after 24 h of incubation period at 37 degrees C.

Dobrzynski P., Li S., Kasperczyk J., Bero M., Gasc F., and Vert M. (2005) Structure-property relationships of copolymers obtained by ring-opening polymerization of glycolide and epsilon-caprolactone. Part 1. Synthesis and characterization. *Biomacromolecules* **6**, 483-488.

Abstract: A series of copolymers with various compositions were synthesized by bulk ring-opening polymerization of glycolide and epsilon-caprolactone, using stannous (II) octoate or zirconium (IV) acetylacetonate as initiator. Reaction time and temperature were varied so as to induce different chain microstructures. The resulting copolymers were characterized by (¹H NMR, SEC, DSC, and X-ray diffraction. The average lengths of glycolyl (L(G)) and caproyl sequences (L(C)) and the degree of randomness (R) were calculated and compared to the values of completely random chains. The concentration of CGC sequences was also obtained which resulted from transesterification reactions. Data

showed that stannous (II) octoate leads to less transesterification than zirconium (IV) acetylacetonate, and lower temperatures lead to less transesterification than higher ones. The copolymers exhibited a more or less blocky chain structure because of the reactivity difference between glycolide and epsilon-caprolactone. The crystalline structure and thermal properties depend on both the composition and the chain microstructure. PGA- and PCL-type crystallites were obtained for copolymers with intermediate compositions.

Eeckman F., Moes A. J., and Amighi K. (2004) Poly(N-isopropylacrylamide) copolymers for constant temperature controlled drug delivery. *Int J Pharm* **273**, 109-119.

Abstract: In the course of the development of a new drug delivery concept, four thermosensitive copolymers of poly(N-isopropylacrylamide) (PNIPAAm), with phase transition temperature slightly higher than 37 degrees C, were synthesised and used as time-controlled drug delivery agents. For this purpose, compression-coated tablets coated with the thermosensitive copolymers and containing Na₂SO₄ were prepared and in vitro dissolution tests were performed at constant physiological temperature, the lag time before drug release being controlled by the amount of Na₂SO₄ incorporated into the form. Due to the salting out effect, the lag time was increased by up to 80-90% for PNIPAAm-co-NVA and PNIPAAm-co-MVA coated tablets.

Eeckman F., Amighi K., and Moes A. J. (2001) Effect of some physiological and non-physiological compounds on the phase transition temperature of thermoresponsive polymers intended for oral controlled-drug delivery. *Int J Pharm* **222**, 259-270.

Abstract: Poly-N-isopropylacrylamide (PNIPAAm) thermosensibility makes this polymer a very attractive candidate for controlled drug delivery systems. The polymer possesses a lower critical solution temperature (LCST) which was found to be around 32 degrees C in pure water, but which can be affected by the medium composition, i.e. presence of salts or surfactants. The knowledge of the effects of such substances on the LCST is very important while using PNIPAAm as a controlled drug delivery agent. The influence of a number of physiological and non-physiological salts and surfactants has been studied. The results obtained show that the addition of salts provokes an important decrease of the LCST of the polymer (salting out effect). A strong influence of the valence and of the size of the anions of the halide group was found. As to the surfactants, according to their type and concentration, a decrease or an increase of the LCST or even no effect at all were found. The effect of the GI secretions on the PNIPAAm phase separation temperature is also discussed.

Eeckman F., Moes A. J., and Amighi K. (2003) Surfactant induced drug delivery based on the use of thermosensitive polymers. *J Control Release* **88**, 105-116.

Abstract: A novel approach of controlled drug delivery using thermosensitive polymers is developed in this paper. The drug release occurs at physiological temperature, at which the polymer is normally not soluble, and no medium temperature changes are required to bring about the delivery. For this purpose benefit is taken from the specific binding properties of some anionic surfactants and poly(N-isopropylacrylamide) (PNIPAAm) in order to modify the dissolution properties of PNIPAAm and of a copolymer with N-vinyl-acetamide (NVA), and so to induce the release of a drug contained in compression coated tablets. The influence of surfactant type and amount on the drug release rates and lag times from tablets coated with PNIPAAm or with the copolymer are discussed. It was found that the lag time is influenced by the surfactant species and amount. When use is made of a copolymer as coating agent, it is possible to bring about the release of the drug by incorporating only a very small amount (as low as 2%) of sodium dodecyl sulfate (SDS) in the coating.

Fairley N., Hoang B. and Allen C. (2008) Morphological control of poly(ethylene glycol)-block-poly(epsilon-caprolactone) copolymer aggregates in aqueous solution. *Biomacromolecules*. **9**, 2283-2291.

Abstract: In aqueous solution, it was found that the amphiphilic copolymer poly(ethylene glycol)-b-poly(caprolactone) (PEG(5000)-b-PCL(4100)) formed different morphologies, including long rod-like, short rod-like, or spherical aggregates, when the copolymer concentration was increased. Nearly identical morphologies were observed with the addition of increasing amounts of PEG(2000)-distearylphosphoethanolamine (PEG(2000)-DSPE) to the copolymer. The morphologies of the aggregates in solution were confirmed by negative stain transmission electron microscopy (TEM) and cryogenic-TEM (cryo-TEM). The critical micelle concentrations of the PEG(5000)-b-PCL(4100) copolymer, PEG(2000)-

DSPE and a mixture of the two materials (PEG(5000)-b-PCL 4100/PEG(2000)-DSPE) were evaluated to determine the thermodynamic stability of the aggregates. Differential scanning calorimetry was performed to gain insight into the degree of mixing of PEG(5000)-b-PCL(4100) and PEG(2000)-DSPE. Overall, combining PEG(5000)-b-PCL(4100) and PEG(2000)-DSPE produced a single population of mixed micelles with rod-like or spherical morphologies depending on the material composition and concentration

Fang Y. and Nishinari K. (2004) Gelation behaviors of schizophyllan-sorbitol aqueous solutions. *Biopolymers* **73**, 44-60.

Abstract: On addition of D-sorbitol, schizophyllan (SPG) aqueous solution forms a thermoreversible gel upon cooling. The gelation process is characterized by rheology, differential scanning calorimetry (DSC), and optical rotation measurement (ORD). It is found that the Winter-Chambon criterion works well in determining the critical gelation point of the present system, although the criterion has been scarcely applicable to systems that show weak-gel properties even before gelation. Moreover, ORD and DSC results indicate that a disordered to ordered conformational change accompanies the gelation process, which is attributed to the transition from SPG triple helix II to I. The gelation temperature of SPG-sorbitol aqueous solution is almost independent of SPG concentration in the examined concentration range and is slightly decreased by lowering SPG molecular weight, while greatly influenced by sorbitol content. The gelation is considered to be induced by the transition from SPG triple helix II to I, which leads to a three-dimensional network constituted by the extremely entangled and stiff SPG triple helices I. Furthermore, it is proved that neither junction zone nor aggregation of SPG triple helices is involved in the SPG-sorbitol gels. The SPG-sorbitol gel is structurally like a solution that is unable to flow within a timescale of usual observation.

Fenniri H., Chun S., Ding L., Zyrianov Y., and Hallenga K. (2003) Preparation, physical properties, on-bead binding assay and spectroscopic reliability of 25 barcoded polystyrene-poly(ethylene glycol) graft copolymers. *J Am Chem Soc* **125**, 10546-10560.

Abstract: Here we describe the preparation of 25 beaded polystyrene-poly(ethylene glycol) graft copolymers from six spectroscopically active styrene monomers: styrene, 2,5-dimethylstyrene, 4-methylstyrene, 2,4-dimethylstyrene, 4-tert-butylstyrene, and 3-methylstyrene. These polymers were thoroughly characterized by Raman, infrared, and $(1)H/(13)C$ NMR spectroscopies, and differential scanning calorimetry. Determination of the swelling properties, peptide synthesis, and on-bead streptavidin-alkaline phosphatase (SAP) binding assay further established that their physical and chemical properties were not significantly altered by the diversity of their encoded polystyrene core. Each of the 25 resins displayed a unique Raman and infrared vibrational fingerprint, which was converted into a "spectroscopic barcode". The position of each bar matches the peak wavenumber in the corresponding spectrum but is independent of its intensity. From this simplified representation similarity maps comparing 35 000 resin pairs were generated to establish the spectroscopic barcoding as a reliable encoding methodology. In effect, in 99% of the cases, the highest similarity coefficients were obtained for resin pairs prepared from the same styrene derivatives even after SAP binding assay. We have also shown that a small but unique combination of a resin's vibrations (30-40%) is sufficient for its identification. However, in rare cases where a resin's vibrational signature has been severely compromised, both the Raman and infrared barcodes were synergistically and reliably utilized to unequivocally identify its chemical make up.

Fraschini C., Jalabert M., and Prud'homme R. E. (2005) Physical characterization of blends of poly(D-lactide) and LHRH (a leuprolide decapeptide analog). *Biomacromolecules* **6**, 3112-3118.

Abstract: Stereocomplexes between poly(D-lactide) (PDLA) and poly(L-lactide) (PLLA) have been extensively studied, including, in recent years, several reports on the stereocomplexation of PDLA with small molecules such as peptides. Here, the possible complexation between PDLA and luteinizing hormone releasing hormone (LHRH), a l-configured decapeptide, is considered for which several observations were made: (1) in calorimetry an additional endothermic peak appears at a lower temperature than the melting temperature of pure PDLA; (2) in Raman analyses a band splitting of the C=O stretching mode (not present in pure PDLA) shows up; (3) in X-ray diffraction, however, no change is observed after mixing the two species, indicating no crystal structure modification (and the absence of any stereocomplex crystal structure). The calorimetric double melting peak is merely explained by the presence of two distinct morphological forms of PDLA, whereas the spectroscopic band splitting can be due to simple differences of crystallinity. From these observations it is concluded that the LHRH modifies the crystallization of PDLA without, however, the formation of a stereocomplex.

Forsyth J. L., Ring S. G., Noel T. R., Parker R., Cairns P., Findlay K., and Shewry P. R. (2002) Characterization of starch from tubers of yam bean (*Pachyrhizus ahipa*). *J Agric Food Chem* **50**, 361-367. **Abstract:** Detailed studies of the starch present in tubers of six accessions of *Pachyrhizus ahipa* (ahipa) have been carried out using starches from tubers of *P. erosus* (Mexican yam bean) and seeds of ahipa and wheat for comparison. Starch accounted for 56-58% of the tuber dry weight with granules occurring in a range of geometric forms and in sizes from below 5 μm to about 35 μm (mean about 10 μm in all accessions except two). The amylose content ranged from 11.6 to 16.8% compared with 16.9% in *P. erosus* tubers and over 23% in the seed starches. X-ray diffraction analysis showed A-type or C(A)-type diffraction patterns. The chain-length distribution of the amylopectin after enzyme debranching showed a peak at DP11 similar to that of wheat starch, but had a less marked shoulder at DP 21-22 and contained a higher proportion of longer chains. Differential scanning calorimetry showed an endothermic peak corresponding to gelatinization with T(max) ranging from 59 to 63 degrees C, which was similar to the T(max) of wheat (about 64 degrees C). The composition of the ahipa starch may mean that it is suitable for food applications that require low amylose content and low retrogradation after processing.

Fustin C. A., Bailly C., Clarkson G. J., De Groote P., Galow T. H., Leigh D. A., Robertson D., Slawin A. M., and Wong J. K. (2003) Mechanically linked polycarbonate. *J Am Chem Soc* **125**, 2200-2207. **Abstract:** The synthesis, by solid-state copolymerization, and characterization of the first polycatenanes based on a commercial polymer are reported. Various amounts of a benzylic amide [2]catenane, the corresponding macrocycle, and a rigid bisphenol fluorene derivative have been quantitatively and homogeneously incorporated into bisphenol A polycarbonate. The resulting copolymers were characterized by size exclusion chromatography coupled with viscosimetry, ^1H NMR, differential scanning calorimetry, and dynamic mechanical analysis. The unexpectedly small influence of [2]catenane incorporation on the glass transition temperature of the copolymers points to remarkable internal mobility of the catenane comonomer rings. A new relaxation linked to the flexible catenane units is also observed. The studies represent a detailed structural characterization of a polymer containing small amounts of mechanical linkages in its backbone and demonstrate that significant effects can be induced by doping conventional polymers with small percentages (2-6% of repeat units) of flexible catenanes.

Gan D. and Lyon L. A. (2001) Tunable swelling kinetics in core-shell hydrogel nanoparticles. *J Am Chem Soc* **123**, 7511-7517.

Abstract: Thermoresponsive, core-shell poly-N-isopropylacrylamide (p-NIPAm) nanoparticles (microgels) have been synthesized by seed and feed precipitation polymerization, and the influence of chemical differentiation between the core and shell polymers on the phase transition kinetics and thermodynamics has been examined. The results suggest that the core-shell architecture is a powerful one for the design of colloidal "smart gels" with tunable properties. To examine these materials, differential scanning calorimetry (DSC), ^1H NMR, and temperature-programmed photon correlation spectroscopy (TP-PCS) have been employed. These measurements show that the addition of small concentrations of a hydrophobic monomer (butyl methacrylate, BMA) into the particle shell produces large decreases in the rate of thermo-induced particle collapse. Conversely, these low levels of hydrophobic modification do not perturb the thermodynamics of the particle phase transition. When these results are examined in light of previous studies of macroscopic hydrogels, they suggest that the formation of a thin, stable skin layer at the particle exterior during the early stages of particle collapse is the rate limiting factor in particle deswelling. Finally, the hydrophobicity (BMA content) of the shell determines the magnitude of the hydrogel collapse rate, while the thickness of the BMA containing region does not impact the observed kinetics. Together, these results suggest that control over the kinetics of microgel deswelling events can be accomplished simply by modification of the particle periphery, and therefore do not require homogeneous modification of the entire polymer structure.

George J., Ramana K. V., Sabapathy S. N., Jagannath J. H., and Bawa A. S. (2005) Characterization of chemically treated bacterial (*Acetobacter xylinum*) biopolymer: Some thermo-mechanical properties. *Int J Biol Macromol* **37**, 189-194.

Abstract: Bacterial cellulose prepared from pellicles of *Acetobacter xylinum* (*Gluconacetobacter xylinus*) is a unique biopolymer in terms of its molecular structure, mechanical strength and chemical stability. The biochemical analysis revealed that various alkali treatment methods were effective in removing proteins and nucleic acids from native membrane resulting in pure cellulose membrane. The effect of various

treatment regimens on thermo-mechanical properties of the material was investigated. The cellulose in the form of purified cellulose membranes was characterized by differential scanning calorimetry (DSC), thermo-gravimetric analysis (TGA) and dynamic mechanical thermal analysis (DMTA). The glass transition temperature (T_g) of the native cellulose (untreated, compressed and dried pellicle) was found to be 13.94 degrees C, in contrast, the chemically treated cellulose membranes has higher T_g values, ranging from 41.41 degrees C to 48.82 degrees C. Investigations on isothermal crystallization were carried out to study the bulk crystallization kinetics. Thermal decomposition pattern of the native as well as alkali treated cellulose was determined by obtaining thermo-gravimetric curves. At higher temperatures (>300 degrees C), the biopolymer was found to degrade. Nevertheless, the alkaline treated cellulose membrane was more stable (between 343.27 degrees C and 370.05 degrees C) in comparison to the native cellulose (298.07 degrees C). Further, the percentage weight loss in case of native cellulose was found to be 26.57%, in comparison to 6.45% for the treated material, at 300 degrees C. The DMTA revealed complex dynamic modulus of the material, at different temperatures and fixed shear stress, applied at a frequency of 5Hz. The study delineated the effect of alkali treatment regimens, on the thermo-mechanical properties of bacterial cellulose for its application over a wide range of temperatures.

Goycoolea F. M., Milas M., and Rinaudo M. (2001) Associative phenomena in galactomannan-deacetylated xanthan systems. *Int J Biol Macromol* **29**, 181-192.

Abstract: The interaction between mesquite seed galactomannan (MSG; D-mannose to D-galactose ratio (M/G) approximately 1.1) and deacetylated xanthan (DX) in 5 mM NaCl leading to synergistic gel formation at 25 degrees C was investigated and compared with the far more studied system made of xanthan and locust bean gum (LBG; M/G approximately 3.5). Rheology and differential scanning calorimetry were used to measure temperatures of gel formation and transition enthalpy as a function of polymer composition, while circular dichroism was used to probe the conformation of DX in the LBG-DX system. MSG and DX associate at 25 degrees C with a well defined stoichiometry of 0.6:1.0 (w/w) at low ionic strength favouring the disordered coil state of DX. When LBG was used in place of MSG in water or 5 mM NaCl, two types of mechanisms of interpolymeric association are envisaged.

Guo W. X. and Huang K. X. (2004) Synthesis and characterization of poly(dimer acid-brassylic acid) copolymer and poly(dimer acid-pentadecandioic acid) copolymer. *Biopolymers* **74**, 248-255.

Abstract: Poly(dimer acid-brassylic acid) [P(DA-BA)] copolymers and poly(dimer acid-pentadecandioic acid) [P(DA-PA)] copolymers were prepared by melt polycondensation of the corresponding mixed anhydride prepolymers. The copolymers were characterized by Fourier transform infrared (FTIR), gel permeation chromatography (GPC), differential scanning calorimetry (DSC), wide angle x-ray powder-diffraction, and thermal gravimetric analysis (TGA). In vitro studies show that all the copolymers are degradable in phosphate buffer at 37 degrees C, and leaving an oily dimer acid residue after hydrolysis for the copolymer with high content of dimer acid. The release profiles of hydrophilic model drug, ciprofloxacin hydrochloride, from the copolymers, follow first-order release kinetics. All the preliminary results suggested that the copolymer might be potentially used as drug delivery devices.

Hoare T. and Pelton R. (2007) Calorimetric analysis of thermal phase transitions in functionalized microgels. *J Phys. Chem B* **111**, 1334-1342.

Abstract: Differential scanning calorimetry (DSC) is used to investigate the thermal phase transitions of a range of N-isopropylacrylamide (NIPAM)-based, carboxylic acid-functionalized microgels with well-defined radial and chain functional group distributions. The transition enthalpies of protonated microgels can be correlated with the hydrophobicity of the functional comonomer, while the transition enthalpies for ionized microgels can be correlated with the degree of microgel deswelling achieved across the thermal phase transition. The peak widths at half-height vary inversely with the average length of NIPAM blocks in each of the microgels, as calculated using a kinetic copolymerization model. Deconvolution of the asymmetric DSC thermograms is accomplished using a two-transition model, thought to relate to core-shell-type transitions induced by the significant local heterogeneities within the functionalized microgels. The ratio between the two transition temperatures of these deconvoluted peaks is a useful quantitative probe of the radial functional group distribution. An additional, low-temperature transition is also observed in the thermogram of the vinylacetic acid-functionalized microgel, indicative of the occurrence of local chain rearrangements prior to the macroscopic phase transition in this microgel. Complementary light scattering analysis suggests that microphase separation may account for this additional transition peak.

Huang D., Simon S. L., and McKenna G. B. (2005) Chain length dependence of the thermodynamic properties of linear and cyclic alkanes and polymers. *J Chem Phys* **122**, 84907.

Abstract: The specific heat capacity was measured with step-scan differential scanning calorimetry for linear alkanes from pentane (C(5)H(12)) to nonadecane (C(19)H(40)), for several cyclic alkanes, for linear and cyclic polyethylenes, and for a linear and a cyclic polystyrene. For the linear alkanes, the specific heat capacity in the equilibrium liquid state decreases as chain length increases; above a carbon number N of 10 (decane) the specific heat asymptotes to a constant value. For the cyclic alkanes, the heat capacity in the equilibrium liquid state is lower than that of the corresponding linear chains and increases with increasing chain length. At high enough molecular weights, the heat capacities of cyclic and linear molecules are expected to be equal, and this is found to be the case for the polyethylenes and polystyrenes studied. In addition, the thermal properties of the solid-liquid and the solid-solid transitions are examined for the linear and cyclic alkanes; solid-solid transitions are observed only in the odd-numbered alkanes. The thermal expansion coefficients and the specific volumes of the linear and cyclic alkanes are also calculated from literature data and compared with the trends in the specific heats.

Huang M. and Fang Y. (2006) Preparation, characterisation and properties of chitosan-g-poly (vinyl alcohol) copolymer. *Biopolymers* **81**, 160-166.

Abstract: The graft copolymer, chitosan-g-poly (vinyl alcohol) with non-toxicity, biodegradability, and biocompatibility, was prepared by a novel method. The copolymer with porous net structure was observed by SEM. It is a potential method to combine chitosan with the synthetic polymers. The grafting reactions were conducted with various poly (vinyl alcohol) (PVA)/ 6-O-succinate-N-phthaloyl-chitosan (PHCSSA) feed ratios to obtain chitosan-g-poly (vinyl alcohol) copolymers with various poly (vinyl alcohol) contents. The chemical structure of the chitosan-g-poly (vinyl alcohol) was characterized by Fourier transform infrared and NMR spectroscopy. DSC, XRD and SEM were also detected to characterize the copolymer. (c) 2005 Wiley Periodicals, Inc. *Biopolymers*, 2005.

Inoue T. and Yamashita K. (2006) Aggregation behavior of polypropylene oxide with electric charges at both ends in aqueous solution. *J Colloid Interface Sci* **300**, 774-781.

Abstract: The aggregation behavior of polypropylene oxide (PPO) with positive charges at both ends was investigated in aqueous solution by means of the measurements of solution turbidity, dynamic light-scattering, differential scanning calorimetry, and dye solubilization. The positive charges were produced by protonation of terminal NH(2) groups attached to the polymer composed of 33 PO units. It was found that the aggregation behavior is quite sensitive to temperature. At low temperature, the polymer dissolves in water as a unimer. When temperature is increased, the unimer solution undergoes a phase separation to give a turbid solution. Further increase in temperature produces a transparent micellar solution. The aggregation of the polymer molecules must be induced by the dehydration of PPO chain caused by temperature increase. According to the analysis of heat absorptions associated with the melting of the solid mixture and the phase separation of the unimer solution, it is suggested that approximately 10% dehydration of PPO chain causes the phase separation. The temperature-composition phase diagram of aqueous mixture of this polymer was constructed on the basis of turbidity and DSC experiments, which reveals the aggregation behavior of this polymer in aqueous medium as a function of concentration and temperature.

Ishihara K., Nomura H., Mihara T., Kurita K., Iwasaki Y., and Nakabayashi N. (1998) Why do phospholipid polymers reduce protein adsorption? *J Biomed Mater Res* **39**, 323-330.

Abstract: The amount of plasma protein adsorbed on a phospholipid polymer having a 2-methacryloyloxyethyl phosphorylcholine (MPC) moiety was reduced compared to the amount of protein adsorbed onto poly[2-hydroxyethyl methacrylate (HEMA)], poly[n-butyl methacrylate (BMA)], and BMA copolymers with acrylamide (AAM) or N-vinyl pyrrolidone (VPy) moieties having a hydrophilic fraction. To clarify the reason for the reduced protein adsorption on the MPC polymer, the water structure in the hydrated polymer was examined with attention to the free water fraction. Hydration of the polymers occurred when they were immersed in water. The differential scanning calorimetric analysis of these hydrated polymers revealed that the free water fractions in the poly(MPC-co-BMA) and poly(MPC-co-n-dodecyl methacrylate) with a 0.30 MPC mole fraction were above 0.70. On the other hand, the free water fractions in the poly(HEMA), poly(AAM-co-BMA), and poly(VPy-co-BMA) were below 0.42. The conformational change in proteins adsorbed on the MPC polymers and poly(HEMA) were determined using ultraviolet and circular dichroism spectroscopic measurements. Proteins adsorbed on poly(HEMA)

changed considerably, but those adsorbed on poly(MPC-co-BMA) with a 0.30 MPC mole fraction differed little from the native state. We concluded from these results that fewer proteins are adsorbed and their original conformation is not changed on polymer surfaces that possess a high free water fraction.

Jeon H. J., Kang M. K., Park C., Kim K. T., Chang J. Y., Kim C. and Song H. H. (2007) Supramolecular ordering of amide dendrons in lyotropic and thermotropic conditions. *Langmuir* **23**, 13109-13116.

Abstract: Self-assembled superstructures of amide dendrons, from first to third generation including monodendrons and covalently linked dimers, were extensively examined, and the supramolecular ordering processes in thermotropic and lyotropic conditions were compared. The superstructures as determined by X-ray diffraction and DSC revealed that the first and second generation dendrons showed nearly identical superstructures regardless of the assembly conditions. But, the third generation dendrons showed a more sensitive self-organizing behavior. The structure obtained from the gel state was lamellar with a more extended conformation, while the structure from the melt state revealed the columnar superstructures of contracted branches. The superstructure formed from the gel state also showed a structural change upon raising the temperature and assumed a structure similar to the thermotropically driven one, implying that the structure formed from the gel is thermodynamically unstable. The formation of lamellar- or cylinder-type superstructures from amide dendrons was primarily dependent on the shape of dendrons, which is associated with the branch size (generation) and the surrounding conditions.

Joralemon M. J., Smith N. L., Holowka D., Baird B., and Wooley K. L. (2005) Antigen-decorated shell cross-linked nanoparticles: synthesis, characterization, and antibody interactions. *Bioconjug Chem* **16**, 1246-1256.

Abstract: Antigen-decorated shell cross-linked knedel-like nanoparticles (SCKs) were synthesized and studied as multivalent nanoscale surfaces from which antibody-binding units were presented in a manner that was designed to approach virus particle surfaces. The SCK nanostructures were fabricated with control over the number of antigenic groups, from mixed micellization of amphiphilic diblock copolymer building blocks that contained either an antigen (2,4-dinitrophenyl) or an ethylpropionate group at the hydrophilic alpha-chain terminus. Amphiphilic diblock copolymers were synthesized by atom transfer radical polymerization of tert-butyl acrylate and methyl acrylate sequentially from either a 2,4-dinitrophenyl-functionalized initiator or ethyl 2-bromopropionate, followed by selective removal of the tert-butyl groups to afford 2,4-dinitrophenyl-poly(acrylic acid)60-b-poly(methyl acrylate)60 (DNP-PAA(60)-b-PMA60) and poly(acrylic acid)70-b-poly(methyl acrylate) (PAA70-b-PMA70). Micelles were assembled via addition of water to THF solutions of the polymers in 0:1, 1:1, and 1:0 molar ratios of DNP-PAA60-b-PMA60 to PAA70-b-PMA70, followed by dialysis against water. The acrylic acid groups of the micelle coronas were partially cross-linked (nominally 50%) with 2,2'-(ethylenedioxy)bis(ethylamine), in the presence of 1-(3'-dimethylaminopropyl)-3-ethylcarbodiimide methiodide. Following extensive dialysis against water, the 0%, 50%, and 100% dinitrophenylated shell cross-linked nanoparticles (DNP-SCKs) were characterized with dynamic light scattering (DLS), transmission electron microscopy (TEM), atomic force microscopy (AFM), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), infrared and UV-vis spectroscopies, and analytical ultracentrifugation (AU). The surface accessibility and bioavailability of the DNP units upon the DNP-SCKs were investigated by performing quenching titrations of fluorescein-labeled IgE antibody in solution and degranulation of IgE sensitized RBL-2H3 cells. The DNP antigens proved to be surface-available and able to form multivalent bonds with IgE antibodies, causing degranulation.

Joralemon M. J., O'Reilly R. K., Hawker C. J., and Wooley K. L. (2005) Shell click-crosslinked (SCC) nanoparticles: a new methodology for synthesis and orthogonal functionalization. *J Am Chem Soc* **127**, 16892-16899.

Abstract: A new methodology for the preparation of well-defined core-shell nanoparticles was developed, based upon the employment of a multifunctional crosslinker to coincidentally stabilize supramolecular polymer assemblies and imbed into the shell unique chemical functionalities. Amphiphilic diblock copolymers of poly(acrylic acid)(80)-b-poly(styrene)(90) that had been assembled into micelles and partially functionalized throughout the corona with alkynyl groups were utilized as Click-readied nanoscaffolds for the formation of shell Click-crosslinked nanoparticles (SCCs). Divergently grown dendrimers of the zero, first, second, and third generations having increasing numbers of azide terminating groups ((N(3))(2)-[G-0], (N(3))(4)-[G-1], (N(3))(8)-[G-2], and (N(3))(16)-[G-3], respectively) were

investigated as crosslinkers via Click reactions with the alkynyl groups to form covalent linkages throughout the block copolymer micelle corona, thus forming a crosslinked shell. The crosslinking reactions were characterized by ^1H NMR and IR spectroscopies, differential scanning calorimetry (DSC), and dynamic light scattering (DLS) measurements. Only the first generation dendrimer ((N(3))(4)-[G-1]) possessed a sufficient balance of polyvalency and water solubility to achieve crosslinking and establish a robust nanostructure. The resulting SCC was further characterized with atomic force microscopy (AFM), transmission electron microscopy (TEM), and analytical ultracentrifugation (AU). The dendritic crosslinker is important as it also allows for the incorporation of excess functionality that can undergo complementary reactions. Within the shell of this SCC the remaining azide termini of the dendrimer crosslinker were then consumed in a secondary Click reaction with an alkynyl-functionalized fluorescein to yield a fluorescently labeled SCC that was characterized with DLS, AFM, TEM, AU, UV-vis, and fluorescent measurements as a function of pH.

Kanya T. C., Sankar K. U., and Sastry M. C. (2003) Physical behavior of purified and crude wax obtained from sunflower (*Helianthus annuus*) seed oil refineries and seed hulls. *Plant Foods Hum Nutr* **58**, 179-196. **Abstract:** The sunflower seed waxes obtained from two sources (i) seed hull as a standard and (ii) crude wax from oil refineries were studied for their crystallization, melting characteristics and morphology of crystals. The results of differential scanning calorimetry of wax obtained from seed hulls showed the melting temperature range of 13.18 degrees C with the onset at 62.32 degrees C, for purified wax, compared to the melting range of 24.73 degrees C with the onset at 42.3 degrees C. for crude wax. The enthalpy of fusion for both waxes were 57.55 kcal/mg and 7.63 kcal/mg, respectively. The DSC melt crystallization temperature range was 15.79 degrees C with the onset of 64.58 degrees C for purified wax and temperature range of 31.45 degrees C with an onset of 57.76 degrees C for crude wax. A similar pattern was observed of wax obtained from the crude wax of oil refineries. The enthalpy of crystallization was -64.27 kcal/mg and -7.67 kcal/mg, respectively. The purified wax obtained from the two sources (i) and (ii) were comparable with completion temperatures of 75.5 degrees C and 75.1 degrees C, respectively. The effect of inhibitor (lecithin) on crystallization of purified wax under light microscope and surface structure by scanning electron microscope were observed. Lecithin at 0.2% inhibited the crystallization but nucleation was unaltered. The wax crystal was inhibited to around 60% of the original size with 0.2% lecithin. It is concluded that the sunflower waxes studied were not comparable in their crystal properties of crude and purified states. Lecithin inhibited the crystallization of sunflower seed wax.

Kelch S., Steuer S., Schmidt A. M. and Lendlein A. (2007) Shape-memory polymer networks from oligo[(epsilon-hydroxycaproate)-co-glycolate]dimethacrylates and butyl acrylate with adjustable hydrolytic degradation rate. *Biomacromolecules*. **8**, 1018-1027.

Abstract: Degradable shape-memory polymer networks intended for biomedical applications were synthesized from oligo[(epsilon-hydroxycaproate)-co-glycolate]dimethacrylates with glycolate contents between 0 and 30 mol % using a photopolymerization process. In addition AB copolymer networks were prepared by adding 60 wt % n-butyl acrylate as comonomer. All synthesized polymer networks are semicrystalline at room temperature. A melting transition $T(m)$ between 18 and 53 degrees C which can be used as switching transition for the shape-memory effect can be attributed to the crystalline poly(epsilon-hydroxycaproate) phase. At temperatures below $T(m)$ the elastic properties are dominated by these physical cross-links. At temperatures higher than $T(m)$ the E modulus of the amorphous polymer networks is lowered by up to 2 orders of magnitude, depending on the chemical cross-link density. Copolymer networks based on macrodimethacrylates with a $M(n)$ of up to 13,500 g x mol⁻¹ and a maximum glycolate content of 21 mol % show quantitative strain recovery rates in stress-controlled cyclic thermomechanical experiments. Hydrolytic degradation experiments of polymer networks performed in phosphate buffer solution at 37 degrees C show that the degradation rate can be accelerated by increasing the glycolate content and decelerated by the incorporation of n-butyl acrylate.

Khalid M. N., Agnely F., Yagoubi N., Grossiord J. L., and Couarraze G. (2002) Water state characterization, swelling behavior, thermal and mechanical properties of chitosan based networks. *Eur J Pharm Sci* **15**, 425-432.

Abstract: Two kinds of chitosan-based hydrogels, a crosslinked chitosan reference gel and a chitosan-poly(ethylene oxide) semi-interpenetrating network (semi-IPN), with potential pH-sensitive swelling and drug delivery properties are characterized. Swelling studies were performed on the two kinds of hydrogels

by differential scanning calorimetry (DSC) at pH 1.2 and by the gravimetric method at pH 1.2 and pH 7.2. Both methods lead to similar results. If pH-dependent swelling properties were observed with both hydrogels, they were however improved for the semi-IPN. The amount of bound water in the xerogels could be determined from DSC measurements and a thermogravimetric analysis. The results obtained by both techniques were in good agreement and indicated that the semi-IPN contained more bound water than the reference gel probably due to the presence of the hydrophilic poly(ethylene oxide) chains. Young modulus of the swollen hydrogels was determined by indentation analysis. The semi-IPN displayed improved mechanical properties compared to the reference gel.

Kim D. Y., Kim Y., and Rhee Y. H. (1998) Bacterial Poly(3-hydroxyalkanoates) Bearing Carbon-Carbon Triple Bonds. *Macromolecules* **31**, 4760-4763.

Abstract: Production of poly(3-hydroxyalkanoates), PHAs, by *Pseudomonas oleovorans* (*P. oleovorans*) and *Pseudomonas putida* (*P. putida*) grown with mixtures of nonanoic acid, NA, and 10-undecynoic acid, 10-UND(identical with), were investigated. Both microorganisms produced PHAs containing carbon-carbon triple bonds in fractions from 0 to 100%, depending on the composition of the carbon substrate mixture. The amounts of unsaturated repeating units in PHAs produced by *P. oleovorans* were higher than those in PHAs produced by *P. putida* grown with the same carbon substrates. The repeating units containing carbon-carbon triple bonds were 3-hydroxy-8-nonynoate, 3HN(&tbd1;), and 3-hydroxy-10-undecynoate, 3HUD(&tbd1;). 3HN(&tbd1;) was the major repeating unit formed from 10-UND(&tbd1;). The relative amounts of 3HN(&tbd1;) and 3HUD(&tbd1;) in PHAs produced by *P. putida* were slightly different from those in PHAs produced by *P. oleovorans*. The number average molecular weights of PHAs produced in this study were approximately 50 000, and polydispersity indices were approximately 2.5 as determined by gel permeation chromatography. The molecular weight distribution and the relative amounts of 3HN(&tbd1;) and 3HUD(&tbd1;) were not affected by either growth time or the composition of the carbon substrate. PHAs bearing triple bonds were soft and differential scanning calorimetry thermograms of these polymers showed very small melting endotherms at approximately 60 degreesC. The glass transition temperatures were in the range of -33 to -21 degreesC.

Kim D. Y., Jung S. B., Choi G. G., Kim Y. B., and Rhee Y. H. (2001) Biosynthesis of polyhydroxyalkanoate copolyester containing cyclohexyl groups by *Pseudomonas oleovorans*. *Int J Biol Macromol* **29**, 145-150.

Abstract: Production of polyhydroxyalkanoates (PHAs) substituted with cyclohexyl groups by *Pseudomonas oleovorans* grown with 4-cyclohexylbutyric acid (4-CHB) and its mixtures with nonanoic acid (NA) was investigated. Addition of NA to medium gave rise to an increase in the total concentration of 3-hydroxy-4-cyclohexylbutyrate repeating unit in the PHAs, indicating that the bioconversion rate of 4-CHB to polyester was significantly improved by the cometabolic effect. Increasing the proportion of NA from 1.0 to 7.5 mM at a concentration of 10 mM total carbon substrate also accelerated the uptake speed of 4-CHB by the organism and resulted in an increase of the ratio of 3-hydroxynonanoate to 3-hydroxyheptanoate from 1.28 to 2.05. Differential scanning calorimetric analysis of the PHAs bearing the corresponding functional groups showed one melting transition and one glass transition temperature varying according to the composition. These results indicated that random copolyesters were obtained from the carbon substrates used in this study.

Klajnert B., Stanislawska L., Bryszewska M., and Palecz B. (2003) Interactions between PAMAM dendrimers and bovine serum albumin. *Biochim Biophys Acta* **1648**, 115-126.

Abstract: Dendrimers are a new class of polymeric materials. They are globular, highly branched, monodisperse macromolecules. Due to their structure, dendrimers promise to be new, effective biomedical materials as oligonucleotide transfection agents and drug carriers. More information about biological properties of dendrimers is crucial for further investigation of dendrimers in therapeutic applications. In this study the mechanism of interactions between polyamidoamine (PAMAM) dendrimers and bovine serum albumin (BSA) was examined. PAMAM dendrimers are based on an ethylenediamine core and branched units are constructed from both methyl acrylate and ethylenediamine. We used three types of PAMAM dendrimers with different surface groups (-COOH, -NH(2), -OH). As BSA contains two tryptophan residues we were able to evaluate dendrimers influence on protein molecular conformation by measuring the changes in the fluorescence of BSA in the presence of dendrimers. Additionally experiments with a fluorescent probe 1-anilinonaphthalene-8-sulfonic acid (ANS) were carried out. The differential scanning

calorimetry (DSC) was chosen to investigate impact on protein thermal stability upon the dendrimers. Our experiments showed that the extent of the interactions between BSA and dendrimers strongly depends on their surface groups and is the biggest for amino-terminated dendrimers.

Kolhe P. and Kannan R. M. (2003) Improvement in ductility of chitosan through blending and copolymerization with PEG: FTIR investigation of molecular interactions. *Biomacromolecules* **4**, 173-180.
Abstract: Chitosan is an important biomaterial used widely in medical applications. One of the key concerns about its use is the fragile nature of chitosan films. By comparing the component molecular interactions using FTIR, this study attempts to understand how the ductility of chitosan can be improved by blending and copolymerizing with poly(ethylene glycol) (PEG). An improvement in ductility was obtained for all compositions of blend as manifested by a decrease in modulus and an increase in strain at break. For comparable PEG composition (approximately 30%), the properties of the solution-cast blend were better than those of the grafted copolymer. Therefore, blending may be a more efficient way to improve ductility of chitosan. FTIR characterization of the materials revealed subtle decreases in molecular interactions upon annealing the partially miscible blend. These may not be apparent in DSC or X-ray diffraction, yet they play a key role in the mechanical behavior. It appears that in the case of the graft copolymer the improvement in the properties comes from suppression of the crystallinity of each component and not from component interactions. On the other hand, in the blend, the improvement appears to come predominantly from the "well-dispersed", "kinetically trapped" phase morphology and from the intermolecular interactions. Therefore, annealing the blend leads to decreased intermolecular interactions, phase coarsening, and deterioration in properties.

Kuo J. H., Lo Y. L., Shau M. D., and Cherng J. Y. (2002) A thermodynamic study of cationic polymer-plasmid DNA complexes by highly-sensitive differential scanning calorimetry. *J Control Release* **81**, 321-325.

Abstract: The characteristics of polymer-DNA complexes formed by positively-negatively charged interaction have a great influence on their transfection potential. Since the limit changes in thermal transitions which were hardly measured in conventional calorimetry, now in this study they have been successfully carried out by highly-sensitive differential scanning calorimetry for better understanding the pDMAEMA-plasmid DNA complexing process. Thermal behaviors of plasmid DNA, polymer and their formed complexes were recorded to give insights into their conformational changes when temperature was raised. In results, the supercoiled or open-circular plasmid DNA is not thermal reversible indicated by the decrease of denaturation peak and disappearance of DNA conformational transition related to its twist status at 50-70 degrees C. The cationic polymer is thermally stable by showing reversible transition peaks after two heating processes. For the cationic polymer-plasmid DNA complexes, electrostatic forces lead to a higher denaturation temperature of plasmid DNA and transition temperature of polymer. Also, heat can cause a topological change in plasmid DNA and then change their mutual complexation capacity.

Lacoulonche F., Chauvet A., Masse J., Egea M. A., and Garcia M. L. (1998) An investigation of FB interactions with poly(ethylene glycol) 6000, poly(ethylene glycol) 4000, and poly-epsilon-caprolactone by thermoanalytical and spectroscopic methods and modeling. *J Pharm Sci* **87**, 543-551.

Abstract: The interactions between flurbiprofen (FB) and different polymers are studied in order to improve the bioavailability of FB. FB-polymer phase diagrams [poly(ethylene glycol) (PEG) 4000, PEG 6000, and poly-epsilon-caprolactone] were constructed and compared with the modeling diagrams. Thermoanalytical methods (differential scanning calorimetry, thermomicroscopy) were used to construct the phase diagrams. Thermodynamic data were used to model the FB-polymer systems. The construction of the FB-polymer phase diagrams showed the existence of a stable invariant called "eutectic" characterized by $(X_E)_{exp}$, $(T_fE)_{exp}$, and $(\Delta H_fE)_{exp}$, the experimental eutectic composition, the experimental temperature, and the enthalpy of eutectic melting, respectively. Modeling confirmed the values for these parameters and was used to evaluate the different Flory-Huggins parameters χ for each FB-polymer mixture. χ values and the infrared spectra confirm that the interactions due to hydrogen bonds between FB and PEG 4000 are more numerous than between FB and PEG 6000 and also more numerous than between FB and poly-epsilon-caprolactone.

Lambeth R. H., Ramakrishnan S., Mueller R., Poziemski J. P., Miguel G. S., Markoski L. J., Zukoski C. F., and Moore J. S. (2006) Synthesis and aggregation behavior of thermally responsive star polymers.

Langmuir **22**, 6352-6360.

Abstract: To mimic the three-dimensional (3-D) globular architecture resulting from the precise positioning of hydrophobic/hydrophilic domains (blocks) of naturally occurring proteins, water-soluble linear and star homopolymers of N,N'-dimethylacrylamide (DMA) were synthesized with prescribed molecular weights via reversible addition-fragmentation chain transfer (RAFT) polymerization and subsequently used as macro chain transfer agents for block copolymerization with N-isopropylacrylamide (NIPAM). For the star block copolymers, the interior block consisted of NIPAM while the exterior block was DMA. Since polyNIPAM thermally switches from hydrophilic to hydrophobic, the 3-D solution conformations of the polymers were studied as a function of temperature using differential scanning calorimetry (DSC), static light scattering (SLS), and dynamic light scattering (DLS). The polymers were observed to form monodisperse aggregates in an aqueous pH 4 buffer solution when heated above the lower critical solution temperature (LCST) of polyNIPAM. The temperature at which the polymers aggregated and the size of the aggregates were dependent on the NIPAM block length and the core architecture. A simple model based on an optimal area per headgroup was used to analyze our experimental findings and was useful for predicting the final size and molecular weight of the aggregates formed.

Lee J. W., Hua F., and Lee D. S. (2001) Thermoreversible gelation of biodegradable poly(epsilon-caprolactone) and poly(ethylene glycol) multiblock copolymers in aqueous solutions. *J Control Release* **73**, 315-327.

Abstract: The multiblock copolymers composed of poly(ethylene glycol)s (PEGs) and biodegradable poly(epsilon-caprolactone)s (PCLs) were synthesized through one-step condensation copolymerization with hexamethylene diisocyanate (HDI) as a coupling agent. The typical phase diagram of these multiblock copolymers in aqueous solution displayed a critical gel concentration (CGC) and an upper phase-transition temperature, which were mainly determined by the PEG/PCL block ratio, the PEG or PCL block lengths and the molecular weight. With decreasing PEG/PCL block ratio, the CGC decreased with an elevated sol-gel transition temperature on account of the enhanced hydrophobicity. The HDI/Diols ratio was used to control the molecular weight. At high molecular weights, the CGC decreased, related to the enhanced aggregation of PCL blocks and physical crosslinkage between PCL block domains due to the increased number of PCL blocks in each molecule. For the sample containing the long PCL(2000) block (M(n), 2000), the CGC dropped dramatically due to the high hydrophobicity and the poor compatibility between PCL and PEG. The dynamic phase transition process was observed by combining optical microscopy (OM) and differential scanning calorimetry (DSC) in a certain heating/cooling rate. Finally, a possible phase separation-induced gelation mechanism is suggested.

Lewis A. L., Berwick J., Davies M. C., Roberts C. J., Wang J. H., Small S., Dunn A., O'Byrne V., Redman R. P., and Jones S. A. (2004) Synthesis and characterisation of cationically modified phospholipid polymers. *Biomaterials* **25**, 3099-3108.

Abstract: Phospholipid-like copolymers based on 2-(methacryloyloxyethyl) phosphorylcholine were synthesised using monomer-starved free radical polymerisation methods and incorporating cationic charge in the form of the choline methacrylate monomer in amounts varying from 0 to 30 wt%, together with a 5 wt% silyl cross-linking agent in order to render them water-insoluble once thermally cured. Characterisation using a variety of techniques including nuclear magnetic resonance spectroscopy, high-pressure liquid chromatography and gel permeation chromatography showed the cationic monomer did not interfere with the polymerisation and that the desired amount of charge had been incorporated. Gravimetric and differential scanning calorimetry methods were used to evaluate the water contents of polymer membranes cured at 70 degrees C, which was seen to increase with increasing cation content, producing materials with water contents ranging from 50% to 98%. Surface plasmon resonance indicated that the coatings swelled rapidly in water, the rate and extent of swelling increasing with increasing cation level. Dynamic contact angle showed that coatings of all the polymers possessed a hydrophobic surface when dry in air, characteristic of the alkyl chains expressed at the surface (>100 degrees advancing angle). Rearrangement of the hydrophilic groups to the surface occurred once wet, to produce highly wettable surfaces with a decrease in advancing angle with increasing cation content. Atomic force microscopy showed all polymer films to be smooth with no features in topographical or phase imaging. Mechanical properties of the dry films were also unaffected by the increase in cation content.

Li S., Dobrzynski P., Kasperczyk J., Bero M., Braud C., and Vert M. (2005) Structure-property relationships of copolymers obtained by ring-opening polymerization of glycolide and epsilon-caprolactone. Part 2. Influence of composition and chain microstructure on the hydrolytic degradation. *Biomacromolecules* **6**, 489-497.

Abstract: A series of glycolide/epsilon-caprolactone copolymers were compression molded and allowed to degrade in a pH 7.4 phosphate buffer at 37 degrees C. Degradation was monitored by various analytical techniques such as (1)H NMR, X-ray diffraction, DSC, CZE, ESI-MS, and inherent viscosity measurements. The results show that the degradation rate depends not only on the copolymer composition but also on its chain microstructure. Generally, copolymers with a higher C-G bond content or a higher degree of randomness exhibit higher degradation rates. Sequences with odd numbers of glycolyl units such as -CGC- and -CGGC-, which result from the second mode transesterification, appear more resistant to hydrolysis. As a consequence, degradation residues obtained at the later stages of degradation are mainly composed of long glycolyl and caproyl sequences linked by -CGC- and -C.

Luo S., Xu J., Zhu Z., Wu C., and Liu S. (2006) Phase transition behavior of unimolecular micelles with thermoresponsive poly(N-isopropylacrylamide) coronas. *J Phys Chem B Condens Matter Mater Surf Interfaces Biophys* **110**, 9132-9139.

Abstract: This paper describes the double phase transition behavior of a thermoresponsive poly(N-isopropylacrylamide) (PNIPAM) brush at the surface of a hydrophobic core. Reversible addition-fragmentation transfer (RAFT) polymerization of N-isopropylacrylamide (NIPAM) was conducted by using a hyperbranched polyester (Boltorn H40) based macroRAFT agent. The resultant multiarm star block copolymer (H40-PNIPAM) exists as unimolecular micelles with hydrophobic H40 as the core, densely grafted PNIPAM brush as the shell. A combination of laser light scattering (LLS) and microdifferential scanning calorimetry (micro-DSC) studies of H40-PNIPAM in aqueous solution reveals double phase transitions of the PNIPAM corona, which is in contrast to the fact that free PNIPAM homopolymer in aqueous solution exhibits a lower critical solution temperature (LCST) at approximately 32 degrees C. The first phase transition takes place in the broad temperature range 20-30 degrees C, which can be tentatively ascribed to the n-cluster-induced collapse of the inner region of the PNIPAM brush close to the H40 core; the second phase transition occurs above 30 degrees C, which can be ascribed to the outer region of PNIPAM brush. Employing the RAFT chain extension technique, the inner and outer part of PNIPAM brush were then selectively labeled with pyrene derivatives, respectively; temperature-dependent excimer fluorescence measurements further support the conclusion that the inner part of PNIPAM brush collapses first at lower temperatures, followed by the collapse of the outer part at higher temperatures.

Ma J., Cao H., Li Y., and Li Y. (2002) Synthesis and characterization of poly(DL-lactide)-grafted gelatins as bioabsorbable amphiphilic polymers. *J Biomater Sci Polym Ed* **13**, 67-80.

Abstract: A series of poly(DL-lactide) grafted gelatins, as new bioabsorbable amphiphilic polymers useful in parenteral drug delivery systems and in tissue engineering, were synthesized by the ring opening polymerization of DL-lactide onto a fractionated gelatin with the molecular weight of 1.02×10^5 . Using tin(II) bis(2-ethylhexanoate) as catalyst, the bulk copolymerization at 140 degrees C and solution copolymerization in dimethylsulfoxide (DMSO) at 80 degrees C were firstly performed in the presence of gelatin. The results showed that the solution copolymerization in DMSO could afford the expected copolymers but the bulk copolymerization would result in an insoluble crosslinked product. The number of grafting sites on gelatin chain could be adjusted by the partial trimethylsilylation of side hydroxy, amino and carboxylic groups in gelatin. The solution copolymerization of DL-lactide on the partially protected gelatin in DMSO was also successful in providing copolymers with different molecular weights. The synthesized copolymers were characterized on the basis of elemental analysis, IR, 1H-NMR and thermal analysis. The IR and 1H-NMR data of these produced copolymers suggested that polylactide branches could be grafted onto gelatin via the side groups such as hydroxyl and amino groups in the solution copolymerization as well as carboxylic groups in bulk copolymerization. The molecular weights of the copolymers could be calculated from the difference of nitrogen contents between a copolymer and free gelatin. The results indicated that molecular weight of the copolymers and those of polylactide branches were increased with the feeding ratio of DL-lactide to gelatin in the copolymerization. However, because of the steric hindrance of some grafting sites on gelatin and the transesterifications of the propagating polylactide branches on gelatin with possibly formed homo-polymeric polylactide chains, the finally formed polylactide branches on gelatin were not very large and the highest average molecular weight of a

polylactide branch was not over 4500 in any solution copolymerizations. The results from the thermal analysis of some copolymers, including thermogravimetry and differential scanning calorimetry, showed that the absorbed water in the samples could be lost at a temperature range below 150 degrees C and melting point decreased with increase of polylactide branches in the poly(DL-lactide)-grafted gelatins.

Maeda T., Kanda T., Yonekura Y., Yamamoto K., and Aoyagi T. (2006) Hydroxylated poly(N-isopropylacrylamide) as functional thermoresponsive materials. *Biomacromolecules* **7**, 545-549.

Abstract: In this study, we developed a poly(N-isopropylacrylamide)-based thermoresponsive polymeric material with a high content of hydroxyl groups. We newly designed the functional monomer, N-(2-hydroxyisopropyl)acrylamide (HIPAAm), considering maintaining the continuous and repeated structure of the isopropylamide group after copolymerization and the monomer reactivity ratios. The thermoresponsive polymer was derived by conventional radical copolymerization of HIPAAm with N-isopropylacrylamide (NIPAAm) in high yield. Estimation of monomer reactivity ratios, $r(1)$ and $r(2)$, supported the almost random sequence of the comonomers. The obtained copolymers showed a very sensitive phase transition and/or separation in response to temperature in aqueous media although they have many hydrophilic parts, and their thermoresponsive behavior was not affected by the pH. Furthermore, the cloud points of these copolymers closely depended on the HIPAAm content and could be easily controlled by adding salts. HIPAAm is expected to regulate the phase transition and/or separation temperature of the NIPAAm-based copolymers while maintaining their desirable sensitive thermoresponse. Differential scanning calorimetric analysis showed that dehydration of the polymer chains occurring in phase transition became incomplete with increasing HIPAAm content. Moreover, it was found that poly(NIPAAm-co-HIPAAm) having a high content of the HIPAAm unit showed liquid-liquid phase separation involving coacervation. The sizes of the coacervate droplets were relatively monodisperse and very minimal. Poly(NIPAAm-co-HIPAAm) is valuable for use in biomedical fields such as bioseparation.

Maeda T., Takenouchi M., Yamamoto K., and Aoyagi T. (2006) Analysis of the Formation Mechanism for Thermoresponsive-Type Coacervate with Functional Copolymers Consisting of N-Isopropylacrylamide and 2-Hydroxyisopropylacrylamide. *Biomacromolecules* **7**, 2230-2236.

Abstract: We now report the formation mechanism of the thermoresponsive-type coacervate with the novel functional temperature-sensitive polymer, poly(N-isopropylacrylamide-co-2-hydroxyisopropylacrylamide) (poly(NIPAAm-co-HIPAAm)), synthesized in our laboratory. The effects of introducing the hydrophilic comonomer (HIPAAm) into the copolymer chains and adding salts on the behaviors of the coacervate droplets induced in the poly(NIPAAm-co-HIPAAm) aqueous solutions were investigated. Not only the particle sizes of the coacervate droplets but also the cloud points of the copolymer solutions could be modulated by the HIPAAm content incorporated in the copolymers. Moreover, the particle sizes of the coacervate droplets were also changed by adding salts. Namely, the particle sizes increased with the decreasing HIPAAm composition and increasing NaCl concentration. In addition, the ^1H NMR and differential scanning calorimetric measurements suggested that as the HIPAAm content decreased or NaCl concentration increased, dehydration of the copolymers induced in the phase transition and/or separation became much easier. Therefore, on the basis of the findings obtained from these measurements, we determined that the particle sizes of the coacervate droplets induced in the temperature-sensitive polymers increased as the number of the water molecules, which are dissociated from the polymeric chains during the phase transition and/or separation, increased. Besides, to examine the separation of the model solutes, the aqueous two-phase separation with the coacervate droplets of poly(NIPAAm-co-HIPAAm) was carried out. The partitions of Methyl Orange as a model solute under both acidic (pH 2) and basic (pH 12) conditions were performed. The amount of Methyl Orange partitioned into the coacervate droplets at pH 12 is much greater than that at pH 2, which indicated that the coacervate droplets could recognize a slight difference in the polarity or structure between the model solutes.

Mata J. P., Majhi P. R., Guo C., Liu H. Z., and Bahadur P. (2005) Concentration, temperature, and salt-induced micellization of a triblock copolymer Pluronic L64 in aqueous media. *J Colloid Interface Sci* **292**, 548-556.

Abstract: The effect of copolymer concentration, temperature, and sodium halides (NaI, NaBr, NaCl, and NaF) on micellization and micellar properties of a poly(ethylene oxide)-block-poly(propylene oxide)-block-poly(ethylene oxide) (PEO-PPO-PEO) amphiphilic copolymer (Pluronic L64: EO(13)PO(30)EO(13)), was examined by different methods such as dye spectral change, Fourier transform

infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), small angle neutron scattering (SANS), dynamic light scattering (DLS), viscosity, and cloud point (CP). Temperature/polymer concentration/salt dependent aggregation behavior of L64 was observed. The data on critical micelle concentration (CMC), critical micelle temperature (CMT), (CP), micelle size, and shape are reported. The Fourier transform infrared (FTIR) showed temperature dependent changes in C-O-C stretching variation band towards higher wave numbers and broadening of band width during the micellization process; this was attributed to increase in proportion of the anhydrous methyl groups, while the proportion of the hydrated methyl groups was decreased. Differential scanning calorimetry (DSC) provides CMTs and CPs from the same experiment. CMC values derived from dye spectral change, decrease significantly with the addition of salt. The increases in salt/copolymer concentration lower the onset temperature of micellization (CMT). Halide anions influence both CMT and CP in the order of F(-) > Cl(-) > Br(-) > I(-) when total salt and copolymer concentration kept constant. SANS results show the increase of inter-micellar interaction due to the increase in temperature/salt concentration; this is supported by viscosity data.

Mata J. P., Majhi P. R., Kubota O., Khanal A., Nakashima K. and Bahadur P. (2008) Effect of phenol on the aggregation characteristics of an ethylene oxide-propylene oxide triblock copolymer P65 in aqueous solution. *J Colloid Interface Sci* **320**, 275-282.

Abstract: The effects of phenol on the micellization, micellar growth, and phase separation of a poly(ethylene oxide)-block-poly(propylene oxide)-block-poly(ethylene oxide) (PEO-PPO-PEO) amphiphilic copolymer (Pluronic P65: EO19 PO30 EO19) in aqueous solution have been studied by cloud point, viscosity, dynamic light scattering (DLS), differential scanning calorimetry (DSC), fluorescence spectroscopy, and small-angle neutron scattering (SANS). Various concentrations of P65 have been chosen to estimate the effect of phenol on different concentration regions of P65. Phenol interacts quite differently at low concentrations (0-2%) than at high concentrations (2-10%) of P65, as per the observation that phenol is more predominant at smaller concentrations of P65. A marked decrease in the cloud points of the P65 solutions is observed in presence of phenol. The critical micelle temperature (CMT) of P65 shows a synergistic effect of phenol on P65 aggregates. Micellar transitions, phase separation, and aggregation behaviours like micellization and micellar growth in the presence of phenol have been observed by combining viscometry, DLS, DSC, and CP. DLS shows that the effect of phenol is predominant at high temperatures. SANS shows a high increase in axial ratio and aggregation numbers in the presence of phenol at fixed concentrations of P65. Fluorescence data illustrate that addition of phenol makes micelles polar but at the same time its favours aggregation. Water-soluble phenol (present in low concentrations) forms aggregates with P65, which can be separated by cloud point extraction, making this study interesting for separation of phenol from the phenol-water system

Matsuoka S., Ogiwara N., and Ishizone T. (2006) Formation of Alternating Copolymers via Spontaneous Copolymerization of 1,3-Dehydroadamantane with Electron-Deficient Vinyl Monomers. *J Am Chem Soc* **128**, 8708-8709.

Abstract: Copolymerizations of 1,3-dehydroadamantane, 1, and various vinyl monomers were carried out in THF at room temperature. On mixing 1 with electron-deficient vinyl monomers, such as acrylonitrile and methyl acrylate, in the absence of any initiator, the copolymerization spontaneously proceeded to give alternating copolymers in 28-88% yield. By contrast, no reaction of 1 occurred at all when isobutyl vinyl ether or styrene was mixed under similar conditions. These contrastive results indicate the high electron density of a central sigma-bond in a strained [3.3.1]propellane derivative, 1. Alternating sequences of the resulting copolymers were characterized by NMR and MALDI-TOF-MS measurements. DSC and TGA measurements revealed the high thermal stability of the alternating copolymers containing bulky, stiff, and strain-free adamantane skeletons.

Mazen F., Milas M., and Rinaudo M. (1999) Conformational transition of native and modified gellan. *Int J Biol Macromol* **26**, 109-118.

Abstract: This paper concerns the characterisation of native gellan by differential scanning calorimetry (DSC) and rheology. The stability of the double helix is characterised by T_m and the enthalpy of conformational change. The role of the external salt concentration is investigated; it is shown that T_m is only slightly modified. At ambient temperature, in 10⁻² M NaCl, native gellan behaves as a loose gel (G' > G''). This behaviour disappears when temperature is larger than 60 degrees C. The comparison with deacylated gellan (commercial sample) shows that the position of conformational transition is much more

influenced by the salt concentration; the helical structure is less stable and the conformational transition presents a hysteresis between heating and cooling runs when the external salt concentration increases. The rheological behaviour is that corresponding to a solution ($G' < G''$) at ambient temperature and in 10^{-2} M NaCl. When the salt excess increases, then a stronger gel is formed. The differences between the two types of samples are clearly established as well as the relations between the conformation and the rheology of the systems.

McCrystal C. B., Ford J. L., and Rajabi-Siahboomi A. R. (1999) Water distribution studies within cellulose ethers using differential scanning calorimetry. 1. Effect of polymer molecular weight and drug addition. *J Pharm Sci* **88**, 792-796.

Abstract: Differential scanning calorimetry (DSC) was employed to characterize the distribution of water in gels produced from a series of hydroxypropylmethylcelluloses (HPMC, Methocel K-series) of different molecular weights (i.e., different viscosity grades). The presence of loosely bound water was characterized as pre-endothermic events occurring at temperatures below the main melting endotherm of free water. Both the magnitude and occurrence of these pre-endothermic events were affected by polymer molecular weight and gel storage time. In addition, the amount of water bound to the polymer depended on polymer molecular weight and gel storage time. The temperature at which frozen water melted within the gels was dependent on polymer concentration, with a depression of extrapolated endothermic melting peak onset occurring with an increase in polymer concentration. The addition of propranolol hydrochloride or diclofenac sodium, as model drugs, affected both the occurrence of pre-endothermic events and the distribution of water within the gels.

McCrystal C. B., Ford J. L., and Rajabi-Siahboomi A. R. (1999) Water distribution studies within cellulose ethers using differential scanning calorimetry. 2. Effect of polymer substitution type and drug addition. *J Pharm Sci* **88**, 797-801.

Abstract: The distribution of water within gels composed of a range of cellulose ether polymers of similar molecular weights (viscosity grades of 4000-6000 cP) but varying substitution types and levels was assessed by differential scanning calorimetry (DSC). Water loosely bound to the polymer was detected as one or more events appearing at the low-temperature side of the main endotherm for the melting of free water in DSC scans. Polymer substitution types and levels, and added drugs (50 mM propranolol hydrochloride or 50 mM diclofenac sodium) influenced the appearance of these melting events. Hydroxypropylcellulose (HPC) and hydroxypropylmethylcellulose (HPMC F4M) gels showed behavior different to that of the other polymers studied. It is thought that any water binding to HPC gels is tightly attached and is not visible as pre-endothermic events on DSC scans. The amount of water bound per polymer repeating unit (PRU) was influenced by and related to the degree of hydrophilic and hydrophobic substitution on the polymer backbone and by the inclusion of either drug. HPC gels had the highest bound water content after 96 h and this was probably related to the high percentage of hydrophilic hydroxypropoxyl substitutions in this polymer. In contrast, methylcellulose (MC A4M) had the lowest bound water content after 96 h storage, and this was explained by the lack of hydrophilic hydroxypropoxyl substitutions in the polymer.

Morello A. P., III, Forbes N. and Mathiowitz E. (2007) Investigating the effects of surfactants on the size and hydrolytic stability of poly(adipic anhydride) particles. *J Microencapsul.* **24**, 40-56.

Abstract: The present study investigates the effects of surfactants (<0.01% v/v) on the size and hydrolytic stability of poly(adipic anhydride) (pAA) micro- and nanospheres fabricated using a modified phase inversion technique. Overall, surfactants increased the output yield by roughly 20%. Lecithin produced the greatest reduction in the volumetric particle size (dvol) compared to particles fabricated with no surfactant (dvol = 530 +/- 300 nm and 2.2 +/- 1.1 microm, respectively). In addition, sorbitan monooleate produced spheres with smaller numeric diameters (dnun) than the control but appeared to induce aggregation (dvol = 7.7 +/- 12.5 microm). The dnun and dvol were not dependent on the hydrophobicity of the surfactant ($R^2 = 0.36$ and 0.03 , respectively) or the apparent surface tension of the non-solvent (NS) phase ($R^2 = 0.44$ and 0.04 , respectively). In addition, quantitative DSC and FT-IR analysis confirmed that altering the particle size could also influence the hydrolytic stability of pAA.

Nair R., Gonen S., and Hoag S. W. (2002) Influence of polyethylene glycol and povidone on the polymorphic transformation and solubility of carbamazepine. *Int J Pharm* **240**, 11-22.

Abstract: PURPOSE: Influence of polymers on the polymorphic transition of drugs has received limited attention in the literature. The main objective of this study was to gain an understanding of the influence of polyethylene glycol and povidone on the crystalline modification and subsequently the solubility of carbamazepine in solid dispersions. METHODS: The physical state of the drug within the dispersions was determined using DSC and powder X-ray diffractometer. DSC and optical microscopy was used to study the kinetics and morphology of dihydrate formation, respectively. RESULTS: Both the polymeric dispersions showed an improved dissolution profile for carbamazepine. Carbamazepine was present in an amorphous form within the povidone dispersions. In contrast, the PEG dispersions showed the presence of crystalline drug. Higher ratios of drug/PEG resulted in the metastable form I of carbamazepine. Dihydrate formation from both the polymeric dispersions was higher compared with pure carbamazepine. The physical state of the drug and the amount of drug in solution accounted for the higher dihydrate formation from these dispersions. CONCLUSIONS: Knowledge of the factors contributing to enhanced solubility is critical to the stability of solid dispersions. Additionally, influence of polymers like povidone on the crystalline transitions of polymorphic drugs may be crucial during its use as a binder in granulation.

Nitta Y., Fang Y., Takemasa M., and Nishinari K. (2004) Gelation of xyloglucan by addition of epigallocatechin gallate as studied by rheology and differential scanning calorimetry. *Biomacromolecules* **5**, 1206-1213.

Abstract: Interaction of tamarind seed xyloglucan (TSX) and epigallocatechin gallate (EGCG) was investigated. TSX alone showed the rheological behaviors of dilute and semidilute solution types in the temperature range from 10 to 50 degrees C and the concentration range from 1 to 10%. Addition of a small amount of EGCG changed the rheological properties of TSX solutions to induce a thermoreversible gelation. The sol-gel transition was detected as a crossover of the storage and loss shear moduli at a certain temperature in thermal scanning rheological measurements and an endo- and exo- thermic peaks in curves obtained by differential scanning calorimetry on heating and cooling. High storage modulus of the gels at all experimental frequencies also indicated the formation of a network structure. Increase in the gel strength and the enthalpy of the transition with increasing EGCG concentration at fixed TSX concentration suggested that EGCG was directly involved in the network formation through association with TSX. The TSX gel was obtained by addition of appropriate amount of EGCG. Addition of an excessive amount of EGCG induced precipitation.

Nomura C.T., Taguchi K., Gan Z., Kuwabara K., Tanaka T., Takase K., and Doi Y. (2005) Expression of 3-ketoacyl-acyl carrier protein reductase (fabG) genes enhances production of polyhydroxyalkanoate copolymer from glucose in recombinant *Escherichia coli* JM109. *Appl Environ Microbiol.* **71**, 4297-306.

Abstract: Polyhydroxyalkanoates (PHAs) are biologically produced polyesters that have potential application as biodegradable plastics. Especially important are the short-chain-length-medium-chain-length (SCL-MCL) PHA copolymers, which have properties ranging from thermoplastic to elastomeric, depending on the ratio of SCL to MCL monomers incorporated into the copolymer. Because of the potential wide range of applications for SCL-MCL PHA copolymers, it is important to develop and characterize metabolic pathways for SCL-MCL PHA production. In previous studies, coexpression of PHA synthase genes and the 3-ketoacyl-acyl carrier protein reductase gene (fabG) in recombinant *Escherichia coli* has been shown to enhance PHA production from related carbon sources such as fatty acids. In this study, a new fabG gene from *Pseudomonas* sp. 61-3 was cloned and its gene product characterized. Results indicate that the *Pseudomonas* sp. 61-3 and *E. coli* FabG proteins have different substrate specificities in vitro. The current study also presents the first evidence that coexpression of fabG genes from either *E. coli* or *Pseudomonas* sp. 61-3 with fabH(F87T) and PHA synthase genes can enhance the production of SCL-MCL PHA copolymers from nonrelated carbon sources. Differences in the substrate specificities of the FabG proteins were reflected in the monomer composition of the polymers produced by recombinant *E. coli*. SCL-MCL PHA copolymer isolated from a recombinant *E. coli* strain had improved physical properties compared to the SCL homopolymer poly-3-hydroxybutyrate. This study defines a pathway to produce SCL-MCL PHA copolymer from the fatty acid biosynthesis that may impact on PHA production in recombinant organisms.

Ogawa E., Takahashi R., Yajima H., and Nishinari K. (2005) Thermally induced coil-to-helix transition of sodium gellan gum with different molar masses in aqueous salt solutions. *Biopolymers* **79**, 207-217.

Abstract: Using 5 samples of well-purified Na-gellans (Na-gellans G1-G5, weight-average molar mass $M(w) = 120 \times 10(3) - 32 \times 10(3)$ at 40 degrees C), the effects of molar mass on the coil-to-double-helix transition in aqueous solutions with 25 mM NaCl were studied by light scattering and circular dichroism (CD) measurements, viscometry, and differential scanning calorimetry (DSC). From the temperature dependence of $M(w)$, molar ellipticity at 201 nm [θ]₂₀₁, intrinsic viscosity [η], and DSC exothermic curves, it was found that the coil-to-double-helix transitions for G1-G5 samples took place at almost the same temperature. The [η] and $M(w)$ obtained in the temperature range from 40 to 25 degrees C can be explained by a simple coil/double-helix equilibrium model using the double-helix contents determined from CD data. The van't Hoff's transition enthalpy $\Delta H(vH)$ of Na-gellans depended on $M(w)$. It is concluded that the coil-to-double-helix transitions of Na-gellans are all-or-none type transitions, and are accelerated with increasing $M(w)$.

Olofsson G., and Wang G. (1998) Isothermal Titration and Temperature Scanning Calorimetric Studies of Polymer-Surfactant Systems in Polymer-Surfactant Systems. Kwak J.C.T. ed., Marcel Dekker Inc. New York, , pp. 317-356.

Pederson E. N., McChalicher C. W., and Srienc F. (2006) Bacterial synthesis of PHA block copolymers. *Biomacromolecules* **7**, 1904-1911.

Abstract: Polyhydroxyalkanoates (PHA) containing block copolymers were synthesized in Cupriavidus necator using periodic substrate addition. Poly(3-hydroxybutyrate) (PHB) segments were formed during fructose utilization. Pulse feeds of pentanoic acid resulted in the synthesis of 3-hydroxyvalerate monomers, forming poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV) random copolymer. PHA synthesis was controlled using analysis of oxygen uptake and carbon evolution rates from the bioreactor off-gas. A combination of characterization techniques applied to the polymer batches strongly suggests the presence of block copolymers: (i) Thermodynamically stable polymer samples obtained by fractionation and analyzed by differential scanning calorimetry (DSC) and nuclear magnetic resonance spectroscopy (NMR) indicate that some fractions, representing approximately 30% of the total polymer sample, exhibit melting characteristics and nearest-neighbor statistics indicative of block copolymers, (ii) preliminary rheology experiments indicate additional mesophase transitions only found in block copolymer materials, (iii) dynamic mechanical analysis shows extension of the rubbery plateaus in block copolymer samples, and (iv) uniaxial extension tests result in differences in mechanical properties (modulus and elongation at failure) expected of similarly prepared block copolymer and single polymer type materials.

Poirier Y., Somerville C., Schechtman L. A., Satkowski M. M., and Noda I. (1995) Synthesis of high-molecular-weight poly([R]-(-)-3-hydroxybutyrate) in transgenic Arabidopsis thaliana plant cells. *Int J Biol Macromol* **17**, 7-12.

Abstract: High-molecular-weight poly([R]-(-)-3-hydroxybutyrate) (PHB), a biodegradable thermoplastic, was produced from a suspension culture of transgenic Arabidopsis thaliana plant cells expressing two genes from the bacterium Alcaligenes eutrophus involved in the synthesis of PHB. The molecular structure of the plant-produced polymer was analysed by gas chromatography, mass spectrometry, proton nuclear magnetic resonance spectroscopy, infra-red spectroscopy, spectropolarimetry, differential scanning calorimetry, X-ray diffraction and size exclusion chromatography. The results indicate that the polymer from transgenic plants appears to have a chemical structure identical to that of PHB produced by bacteria. However, the molecular weight distribution of the plant-produced PHB was much broader than that of typical bacterial PHB.

Ramachander T. V., Rohini D., Belhekar A., and Rawal S. K. (2002) Synthesis of PHB by recombinant E. coli harboring an approximately 5 kb genomic DNA fragment from Streptomyces aureofaciens NRRL 2209. *Int J Biol Macromol* **31**, 63-69.

Abstract: An approximately 5.0 kb Sau3A I genomic DNA fragment from Streptomyces aureofaciens NRRL 2209 was cloned in a plasmid vector and introduced into Escherichia coli. The recombinant E. coli accumulated polyhydroxyalkanoates (PHAs) as cytoplasmic inclusions. The accumulated PHA was identified as the isotactic homopolymer of PHB with a molecular weight of 2.85×10^5 . Purified PHB granules were spherical with an average size of 1.1 μm and of stable configuration. DSC thermogram suggested high crystalline nature of the polymer. Maximum thermal degradation of the biopolymer

occurred between 250 and 340 degrees C. Recombinant E. coli cells preferentially utilized glycerol as the carbon source and accumulated 25-28 times more PHB than the native S. aureofaciens.

Ramakrishnan M., Sheeba V., Komath S. S., and Swamy M. J. (1997) Differential scanning calorimetric studies on the thermotropic phase transitions of dry and hydrated forms of N-acylethanolamines of even chainlengths. *Biochim Biophys Acta* **1329**, 302-310.

Abstract: N-acylethanolamines (NAEs) have attracted the attention of researchers in the last two decades due to their occurrence in biological membranes under conditions of stress as well as under normal conditions. Differential scanning calorimetric studies have been carried out on dry and hydrated samples of a homologous series of N-acylethanolamines containing saturated acyl chains of even number of carbon atoms ($n = 8-20$). In both cases a major sharp endothermic transition was observed which occurs at the melting point for the dry NAEs whereas for the hydrated samples it occurs at considerably lower temperatures. The enthalpies and entropies corresponding to this transition could be fitted, in each case, to a straight line suggesting that the transition enthalpy and transition entropy consist of a fixed component from the polar head group and the terminal methyl group, whereas the contribution of the methylene groups, $(CH_2)_n$, is linearly proportional to the number of carbon atoms in it. The contributions of each methylene unit to the transition enthalpy and transition entropy of NAEs were found to be $\Delta H(\text{inc}) = 0.82$ (± 0.02) and 0.96 (± 0.06) kcal mol^{-1} , and $\Delta S(\text{inc}) = 2.01$ (± 0.06) and 2.37 (± 0.17) $\text{cal mol}^{-1} \text{K}^{-1}$, respectively, for the dry and hydrated samples of NAEs, whereas the end contributions arising from the head group and the terminal methyl group were determined to be $\Delta H(\text{o}) = -0.10$ (± 0.26) and -0.52 (± 0.82) kcal mol^{-1} and $\Delta S(\text{o}) = 2.12$ (± 0.71) and 3.1 (± 2.3) $\text{cal mol}^{-1} \text{K}^{-1}$, respectively, for the dry and hydrated samples of NAEs. These results are relevant to an understanding of the thermodynamics of the phase properties of NAEs in membranes.

Rodriguez-Abreu C., Shrestha L. K., Varade D., Aramaki K., Maestro A., Quintela A. L. and Solans C. (2007) Formation and properties of reverse micellar cubic liquid crystals and derived emulsions. *Langmuir* **23**, 11007-11014.

Abstract: The structure of the reverse micellar cubic (I2) liquid crystal and the adjacent micellar phase in amphiphilic block copolymer/water/oil systems has been studied by small-angle X-ray scattering (SAXS), rheometry, and differential scanning calorimetry (DSC). Upon addition of water to the copolymer/oil mixture, spherical micelles are formed and grow in size until a disorder-order transition takes place, which is related to a sudden increase in the viscosity and shear modulus. The transition is driven by the packing of the spherical micelles into a Fd3m cubic lattice. The single-phase I2 liquid crystals show gel-like behavior and elastic moduli higher than 104 Pa, as determined by oscillatory measurements. Further addition of water induces phase separation, and it is found that reverse water-in-oil emulsions with high internal phase ratio and stabilized by I2 liquid crystals can be prepared in the two-phase region. Contrary to liquid-liquid emulsions, both the elastic modulus and the viscosity decrease with the fraction of dispersed water, due to a decrease in the crystalline fraction in the sample, although the reverse emulsions remain gel-like even at high volume fractions of the dispersed phase. A temperature induced order-disorder transition can be detected by calorimetry and rheometry. Upon heating the I2 liquid crystals, two thermal events associated with small enthalpy values were detected: one endothermic, related to the "melting" of the liquid crystal, and the other exothermic, attributed to phase separation. The melting of the liquid crystal is associated with a sudden drop in viscosity and shear moduli. Results are relevant for understanding the formation of cubic-phase-based reverse emulsions and for their application as templates for the synthesis of structured materials.

Rodriguez-Cabello J. C., Alonso M., Perez T., and Herguedas M. M. (2000) Differential scanning calorimetry study of the hydrophobic hydration of the elastin-based polypentapeptide, poly(VPGVG), from deficiency to excess of water. *Biopolymers* **54**, 282-288.

Abstract: The polypentapeptide of elastin, poly(VPGVG), has become an interesting model polypeptide in understanding the mechanism of protein folding and assembly. Due to its simple amino acid composition and the predominance of apolar side chains, this polymer shows strong hydrophobic-hydration phenomena. This paper explores, by calorimetric methods, the nature and structure of the clathrate-like arrangements that take place, surrounding the apolar side chains of the polymer. The performance of these methods, especially differential scanning calorimetry, has a well-gained reputation. In this work, the development of the clathrate-like structures around this model polymer has been followed from water deficiency to water-

excess states. Two main conclusions have been obtained from the data obtained. First, there is an upper limit of about 170 water molecules per pentamer as the number of water molecules required to form all the possible clathrate-like structures. Second, these structures exist as an inhomogeneous population with energies spreading in a significantly broad range, which is likely related to differences in geometrical parameters (bond lengths and angles) of the clathrate structure. Copyright 2000 John Wiley & Sons, Inc.

Roux E., Lafleur M., Lataste E., Moreau P., and Leroux J. C. (2003) On the characterization of pH-sensitive liposome/polymer complexes. *Biomacromolecules* **4**, 240-248.

Abstract: A randomly alkylated copolymer of N-isopropylacrylamide, methacrylic acid and N-vinyl-2-pyrrolidone was characterized with regard to its pH- and temperature-triggered conformational change. It was then complexed to liposomes to produce pH-responsive vesicles. Light scattering and differential scanning calorimetry experiments performed at neutral pH revealed that the polymer underwent coil-to-globule phase transition over a wide range of temperatures. At 37 degrees C and pH 7.4, although the polymer was water-soluble, Fourier transform infrared spectroscopy analysis showed that it was partly dehydrated. At acidic pH, the decrease in the lower critical solution temperature was accompanied by an increase in cooperativity degree of the phase transition. Complexation of copolymer to liposomes did not substantially influence its phase transition. The liposome/copolymer complexes were stable at neutral pH but rapidly released their contents under acidic conditions. The copolymer slightly increased liposome circulation time following intravenous administration to rats. The addition of poly(ethylene glycol) to the formulation had a detrimental effect on pH-sensitivity but enhanced substantially the circulation time.

Ruiz L., Fine E., Voros J., Makohliso S. A., Leonard D., Johnston D. S., Textor M., and Mathieu H. J. (1999) Phosphorylcholine-containing polyurethanes for the control of protein adsorption and cell attachment via photoimmobilized laminin oligopeptides. *J Biomater Sci Polym Ed* **10**, 931-955.

Abstract: In this study, we synthesized a biomaterial whose surface inhibits non-specific protein and cell attachment. The polymer was designed to mimic the external cell plasma membrane properties through the introduction of particular chemical constituents of the cell membrane: phospholipid polar headgroups. This was done by copolymerizing phosphorylcholine (PC) groups into a polyurethane polymer backbone (PCPUR). Peptides known to induce specific cell attachment were subsequently bound to the surface of this copolymer in a photoaddressable manner to obtain surfaces that allowed the attachment of cells in a specific pattern. Two polymers with different phosphorylcholine concentrations were synthesized and their bulk and surface properties were characterized through differential scanning calorimetry, wettability measurements, angle-resolved X-ray photoelectron spectroscopy and time-of-flight secondary ion mass spectrometry. Protein and lipid adsorption investigation using optical waveguide light mode spectroscopy showed that the irreversible adsorption of both proteins and lipids is drastically reduced as a result of simultaneous contributions of the PC groups, molecular mobility and strong hydrophilicity of the polymers. Consequently, this leads to a marked reduction in the cellular attachment response, which further decreases with increasing PC concentration. Finally, when the polymer surface was photo-derivatized, attachment of the neural NG108-15 cell line occurred only on the areas of the PCPUR where the laminin CDPGYIGSR peptide sequence was photoimmobilized. Cell attachment was nevertheless found to be non-specific with respect to the peptide sequence used and reasons for such results are therefore discussed.

Ryu J. H., Oh N. K., Zin W. C., and Lee M. (2004) Self-assembly of rod-coil molecules into molecular length-dependent organization. *J Am Chem Soc* **126**, 3551-3558.

Abstract: A series of rod-coil molecules (n-x, where n represents the number of repeating units in a PPO coil and x the number of phenyl groups in a rod segment) with variation in the molecular length, but an identical rod to coil volume ratio was synthesized, and their self-assembling behavior was investigated by using DSC and X-ray scatterings. The molecule with a short rod-coil molecule (16-4) shows a 3-D tetragonal structure based on a body-centered symmetry of the discrete bundles in addition to a lamellar structure. This 3-D lattice, on heating, collapses to generate a disordered micellar structure. Remarkably, the molecules based on longer molecular length (21-5 and 24-6) were observed to self-organize into, on heating, lamellar, tetragonally perforated lamellar, 2-D hexagonal columnar and finally disordered micellar structures. Further increase in the molecular length as in the case of 29-7 and 32-8 induces a 3-D hexagonally perforated lamellar structure as an intermediate structure between the lamellar and tetragonally perforated lamellar structures. Consequently, these systems demonstrate the ability to regulate the domain

nanostructure, from 2-dimensionally continuous layers, long strips to discrete bundles via periodic perforated layers by small changes in the molecular length, at an identical rod-to-coil volume fraction.

Taddei P., Tugnoli V., Bottura G., Dallavalle E., and Zechini D. A. (2002) Vibrational, ¹H-NMR spectroscopic, and thermal characterization of gladiolus root exudates in relation to *Fusarium oxysporum* f. sp. *gladioli* resistance. *Biopolymers* **67**, 428-439.

Abstract: Fourier transform Raman (FT Raman) and IR (FTIR) and (¹H)-NMR spectroscopies coupled with differential scanning calorimetry (DSC) were applied to the characterization of root exudates from two cultivars of gladiolus (Spic Span and White Prosperity) with different degrees of resistance and susceptibility to *Fusarium oxysporum gladioli*, the main pathogen of gladiolus. This work was aimed at correlating the composition of root exudates with the varietal resistance to the pathogen. Spectroscopic analysis showed that White Prosperity root exudate differs from Spic Span root exudate by a higher relative amount of the aromatic-phenolic and sugarlike components and a lower relative amount of carbonylic and aliphatic compounds. DSC analysis confirmed the spectroscopic results and showed that White Prosperity root exudate is characterized by an aromatic component that is present in a higher amount than in the Spic Span root exudate. The results are discussed in relation to the spore germination tests showing that White Prosperity, which is characterized by a remarkable resistance toward *F. oxysporum gladioli*, exudes substances having a negative influence on microconidial germination of the pathogen; root exudates from Spic Span, one of the most susceptible cultivars to *F. oxysporum gladioli*, proved to have no effect. White Prosperity's ability to inhibit conidial germination of *F. oxysporum gladioli* can be mainly related to the presence of a higher relative amount of aromatic-phenolic compounds.

Takahashi K., Kondo H., Kuroiwa H., Yokote Y., and Hattori M. (2000) Reversible thermal transition of soluble branched chains from slightly acid-treated potato starch. *Biosci Biotechnol Biochem* **64**, 1365-1372.

Abstract: The reversible thermal transition of soluble branched starch chains prepared from slightly acid-treated potato starch granules (ATS) was investigated. Potato starch was immersed in 15% sulfuric acid to obtain ATS with a 1% hydrolysis rate. About half of the molecules of ATS, which spontaneously formed large aggregates with a mass of a few million daltons in aqueous solution, was fractionated and soluble branched starch chains with a relative molecular weight (*M_r*) of 8.91×10^4 were obtained. Structural analysis indicated that the soluble branched starch chains consisted of three unit chains with *M_r* 7,900 and 21 unit chains with *M_r* 2,700. DSC and FT-IR measurements showed that the soluble branched starch chains underwent a reversible thermal transition, which is considered to be a helix-coil transition, during heating and cooling, but a debranched sample and beta-limit dextrans showed substantially different thermal behavior, indicating the contribution of the ordered structure of the branched chains.

Tanaka M., Rehfeldt F., Schneider M. F., Gege C., Schmidt R. R., and Funari S. S. (2005) Oligomer-to-Polymer transition in short ethylene glycol chains connected to mobile hydrophobic anchors. *Chemphyschem* **6**, 101-109.

Abstract: We studied the structure of short ethylene glycol (EG) chains with *N* repeating units (EGN, *N* = 3, 6, 9, 12, and 15) connected to hydrophobic dihexadecyl chains by means of a combination of differential scanning calorimetry (DSC) and small- and wide-angle X-ray scattering (SAXS/WAXS). These synthetic amphiphiles dispersed in water form planar lamellar stacks and hexagonal cylinders confining the EG chains to restricted geometries. Owing to the self-assembly of the anchoring points, the lateral density of EG chains in planar lamella can be quantitatively controlled. Furthermore, the chain-melting phase transition of the anchors enables us to "switch" the intermolecular distance reversibly. SAXS/WAXS results suggest that the shorter EG chains (*N* = 3, 6, and 9) assume a helical conformation in stacks of planar lamella. When the EG chains are further elongated (*N* = 12 and 15), the lamellar periodicities cannot be explained by a linear extrapolation of shorter oligomers, but can be interpreted well as polymer brushes following the scaling theorem. Such rich phase behaviors of EGN molecules can be used as a simple model of oligo/poly-saccharide chains on cell surfaces, which act not only as flexible repellers between neighboring cells but also as stable spacers for functional ligands.

Thunemann A. F., Kubowicz S., Burger C., Watson M. D., Tchegotareva N., and Mullen K. (2003) Alpha-helical-within-discotic columnar structures of a complex between poly(ethylene oxide)-block-poly(l-lysine) and a hexa-peri-hexabenzocoronene. *J Am Chem Soc* **125**, 352-356.

Abstract: Poly(ethylene oxide)-block-poly(l-lysine) (PEO-PLL) was complexed with an amphiphilic hexa-

peri-hexabenzocoronene (HBC). This produced a thermotropic liquid crystalline material (PEO-PLL-HBC), which was investigated by FTIR spectroscopy and differential scanning calorimetry as well as by wide- and small-angle X-ray scattering. It was found that the poly(L-lysine) blocks form an alpha-helical secondary structure. Each helix is surrounded symmetrically by six discotic columns of HBC, which gives an alpha-helical-within-discotic column structural entity. The dense packing of these entities produces hexagonal sublattices (formed by the columns) in the frame of a two-dimensional hexagonal lattice (formed by the helices). An order-order transition from a columnar structure Col1 to Col2 was found at 54 degrees C. The unit cell constants are 5.75 nm (Col1) and 6.60 nm (Col2). The larger unit cell size of Col2 was explained by a higher intracolumnar order of the latter in which the packing distance of the disklike HBC cores is well-defined (0.353 nm). PEO-PLL-HBC combines essential features of liquid crystals with a basic structural element of proteins into a single material.

Tsuji H. and Tezuka Y. (2005) Alkaline and enzymatic degradation of L-lactide copolymers, 1. Amorphous-made films of L-lactide copolymers with D-lactide, glycolide, and epsilon-caprolactone. *Macromol Biosci* **5**, 135-148.

Abstract: Films of poly(L-lactide) [i.e., poly(L-lactic acid) (PLLA)] and L-lactide copolymers with glycolide [P(LLA-GA)(81/19)], epsilon-caprolactone [P(LLA-CL)(82/18)], D-lactide [P(LLA-DLA)(95/5), (77/23), and (50/50)] were prepared and a comparative study on the effects of comonomer type and content on alkaline and proteinase K-catalyzed hydrolyses of the films was carried out. The hydrolyzed films were investigated using gravimetry (weight loss and water absorption), differential scanning calorimetry (DSC), polarimetry, and gel permeation chromatography (GPC). To exclude the effects of molecular weight and crystallinity on the hydrolysis, the films were prepared from polymers having similar molecular weights and made amorphous by melt-quenching. It was found that incorporation of hydrophilic glycolide units in L-lactide chains raises the alkaline and enzymatic hydrolyzabilities, whereas incorporation of hydrophobic epsilon-caprolactone units in L-lactide chains reduces the alkaline and enzymatic hydrolyzabilities. On the other hand, incorporation of D-lactide units with the same hydrophilicity of L-lactide units increases the alkaline hydrolyzability but decreases the enzymatic hydrolyzability. The alkaline hydrolyzability of the films of L-lactide copolymers with different kinds of comonomers and P(LLA-DLA) with different D-lactide unit contents can be closely related to their hydrophilicity. On the other hand, the enzymatic hydrolyzability of L-lactide copolymer films with different kinds of comonomers is mainly determined by hydrophilicity, while that of P(LLA-DLA) films is determined by the averaged L-lactyl and D-lactyl unit sequence lengths. The catalytic effect of proteinase K relative to that of alkali on the hydrolysis of P(LLA-DLA)(77/23) and P(LLA-GA)(81/19) films normalized by that of PLLA was lower than unity, whereas the normalized relative catalytic effect of proteinase K on the hydrolysis of P(LLA-CL)(82/18) film was higher than unity, meaning that despite low absolute alkaline and enzymatic hydrolyzability of the P(LLA-CL)(82/18) film, the catalytic effect of proteinase K may be maintained for this copolymer film, probably because of its blocky structure.

Tsuji H., Miyase T., Tezuka Y., and Saha S. K. (2005) Physical properties, crystallization, and spherulite growth of linear and 3-arm poly(L-lactide)s. *Biomacromolecules* **6**, 244-254.

Abstract: The physical properties, crystallization, and spherulite growth behavior and mechanism of linear and 3-arm poly(L-lactide) [i.e., poly(L-lactic acid) (PLLA)] have been investigated using absolute molecular weight as a molecular index. The branching reduces the chain mobility of PLLA and must be excluded from the crystalline regions. The former factor gives the higher glass transition temperature ($T(g)$) and starting temperature for thermal degradation ($T(d,S)$) of 3-arm PLLA compared with those of linear PLLA. On the other hand, both the former and the latter factors lead to the higher cold crystallization temperature ($T(cc)$), the longer induction period for spherulite growth ($t(i)$), the lower melting temperature ($T(m)$), crystallinity ($X(c)$), and radius growth rate of the spherulites (G) for the 3-arm PLLA compared with those for the linear PLLA. The G of 3-arm PLLA showed the vague dependence on number-average molecular weight ($M(n)$), probably because the branching effect was balanced with the molecular weight effect. At the $M(n)$ exceeding critical values, the linear and 3-arm PLLA crystallize in regime II or regime III kinetics, depending on crystallization temperature ($T(c)$). In contrast, at the $M(n)$ below critical values, the linear and 3-arm PLLA crystallize according solely to regime III and regime II kinetics, respectively, for all the $T(c)$.

van d., V, Antipova A. S., Rollema H. S., Burova T. V., Grinberg N. V., Pereira L., Gilsenan P. M., Tromp R. H., Rudolph B., and Grinberg V. Y. (2005) The structure of kappa/iota-hybrid carrageenans II. Coil-helix transition as a function of chain composition. *Carbohydr Res* **340**, 1113-1129.

Abstract: This paper describes the effect of the kappa/iota-ratio on the physical properties of kappa/iota-hybrid carrageenans (synonyms: kappa-2, kappa-2, weak kappa, weak gelling kappa). To this end, a series of kappa/iota-hybrid carrageenans ranging from almost homopolymeric kappa-carrageenan (98 mol-% kappa-units) to almost homopolymeric-carrageenan (99 mol-% iota-units) have been extracted from selected species of marine red algae (Rhodophyta). The kappa/iota-ratio of these kappa/iota-hybrids was determined by NMR spectroscopy. Their rheological properties were determined by small deformation oscillatory rheology. The gel strength (storage modulus, G') of the kappa/iota-hybrids decreases with decreasing kappa-content. On the other hand, the gelation temperature of the kappa-rich kappa/iota-hybrids is independent of their composition. This allows one to control the gel strength independent of the gelation or melting temperature. The conformational order-disorder transition of the kappa/iota-hybrids was studied using optical rotation and high-sensitivity differential scanning calorimetry. High-sensitivity DSC showed that the total transition enthalpy of the kappa/iota-hybrids goes through a minimum at 60 mol-% kappa-units, whereas for the mixture of kappa- and iota-carrageenan, the total transition enthalpy is a linear function of the composition. With respect to the ordering capability, the kappa/iota-hybrid carrageenans seem to behave as random block copolymers with length sequence distributions truncated from the side of the small lengths. Intrinsic thermodynamic properties (e.g., transition temperature and enthalpy) of kappa- and iota-sequences in these copolymers are close to those of their parent homopolymers. The critical sequence length for kappa-sequences is 2-fold of that for iota-sequences.

van d., V, Rollema H. S., Grinberg N. V., Burova T. V., Grinberg V. Y., and Tromp R. H. (2002) Coil-helix transition of iota-carrageenan as a function of chain regularity. *Biopolymers* **65**, 299-312.

Abstract: A series of iota-carrageenans containing different amounts of nu-carrageenan (0-23 monomer %) have been prepared from neutrally extracted carrageenan of *Eucheuma denticulatum*. nu-Carrageenan is the biochemical precursor of iota-carrageenan. The conformational order-disorder transition and rheological properties of these carrageenans were studied using optical rotation, rheometry, size exclusion chromatography coupled to multiangle laser light scattering, and high-sensitivity differential scanning calorimetry. The helix forming capacity of iota-carrageenan turns out to decrease monotonously with increasing amount of nu-units. In contrast, the rheological properties of iota-carrageenan are remarkably enhanced by the presence of a small amount of nu-units, yielding a maximum twofold increase in G' at 3% nu-units. It is concluded that the structure-forming capacity of iota-carrageenan, containing a small amount of nu-carrageenan, is significantly higher than that of pure iota-carrageenan. This phenomenon is explained in terms of the balance between the helical content and the number of cross-links between chains, taking into consideration the fact that nu-units introduce "kinks" in the chain conformation enabling neighboring chains to connect. Increasing amounts of nu-units increase the number of cross-links in the network, resulting in increased gel strength. On the other hand, a reduced length of the helical strands weakens the cross-links between the different chains and, consequently, the gel.

Wang F., Bronich T. K., Kabanov A. V., Rauh R. D., and Roovers J. (2005) Synthesis and evaluation of a star amphiphilic block copolymer from poly(epsilon-caprolactone) and poly(ethylene glycol) as a potential drug delivery carrier. *Bioconjug Chem* **16**, 397-405.

Abstract: A star polymer composed of amphiphilic block copolymer arms has been synthesized and characterized. The core of the star polymer is polyamidoamine (PAMAM) dendrimer, the inner block in the arm is lipophilic poly(epsilon-caprolactone) (PCL), and the outer block in the arm is hydrophilic poly(ethylene glycol) (PEG). The star-PCL polymer was synthesized first by ring-opening polymerization of epsilon-caprolactone with a PAMAM-OH dendrimer as initiator. The PEG polymer was then attached to the PCL terminus by an ester-forming reaction. Characterization with SEC, ^1H NMR, FTIR, TGA, and DSC confirmed the star structure of the polymers. The micelle formation of the star copolymer (star-PCL-PEG) was studied by fluorescence spectroscopy. Hydrophobic dyes and drugs can be encapsulated in the micelles. A loading capacity of up to 22% (w/w) was achieved with etoposide, a hydrophobic anticancer drug. A cytotoxicity assay demonstrated that the star-PCL-PEG copolymer is nontoxic in cell culture. This type of block copolymer can be used as a drug delivery carrier.

Wang L., Venkatraman S., Gan L. H., and Kleiner L. (2005) Structure formation in injectable poly(lactide-co-glycolide) depots. II. Nature of the gel. *J Biomed Mater Res B Appl Biomater* **72**, 215-222.

Abstract: The benzyl benzoate solutions of poly(D,L-lactide-co-glycolide), a random oriented synthesized copolymer with L/G ratio of 50:50, have been shown to form gels during aging and upon injection into buffer or water. The gelation properties influence drug release kinetics for these injectable, depot-forming solutions. In this article, we report on the mechanism of gelation. We find that only polymers that have a certain average block length of glycolide units form gels during aging as well as depots upon in vitro. Thus, gel formation is likely due to the formation of ordered solvated aggregates of blocky glycolide units. Rheometry, differential scanning calorimetry, and nuclear magnetic resonance were used to investigate the gelation kinetics and the polymer molecular parameters. Of all the polymers used, poly(lactide-co-glycolide)s with glycolide average block length <2.9 did not show any gelation behavior. The details of the gelation process are also solvent dependent.

Weng Y., Ding Y., and Zhang G. (2006) Microcalorimetric Investigation on the lower critical solution temperature behavior of N-isopropylacrylamide-co-acrylic acid copolymer in aqueous solution. *J Phys Chem B Condens Matter Mater Surf Interfaces Biophys* **110**, 11813-11817.

Abstract: The lower critical solution temperature (LCST) behaviors of random and segmented copolymers of N-isopropylacrylamide (NIPAM) and acrylic acid (AA) prepared in dioxane and water have been investigated by using ultrasensitive microcalorimetry (US-DSC). The introduction of AA increases the LCST of the former but slightly affects that of the latter. When the molar fraction of AA is low (approximately 2 mol %), the LCST of the segmented copolymer shifts to a higher temperature with increasing pH, while the LCST of the corresponding random copolymer slightly changes. Below the boiling point of water, the random copolymer and segmented copolymer with the molar fraction of AA about 15 mol % no longer exhibit an LCST at pH > 5. The addition of calcium ions leads the LCST of both the segmented copolymer and random copolymer to decrease. Our results suggest that the LCST behavior of the copolymers is determined by the clustering of poly(N-isopropylacrylamide) segments.

Xu X. D., Zhang X. Z., Yang J., Cheng S. X., Zhuo R. X. and Huang Y. Q. (2007) Strategy to introduce a pendent micellar structure into poly(N-isopropylacrylamide) hydrogels. *Langmuir* **23**, 4231-4236.

Abstract: A novel class of functional poly(N-isopropylacrylamide) (PNIPAAm) hydrogels with pendent micellar structure resulting from the pending amphiphilic polymers was designed and prepared. The influence of the pendent micellar structure on the properties of the resulted PNIPAAm hydrogels was examined in terms of morphology observed by scanning electron microscopy, thermal response through differential scanning calorimetry, and deswelling/reswelling kinetics upon external temperature changes. In comparison with the conventional ones, the novel PNIPAAm hydrogels with pendent micellar structure presented improved temperature-sensitive properties, i.e., enlarged water containing capability at room temperature, as well as improved deswelling rate upon heating.

Yoon S. C. and Choi M. H. (1999) Local sequence dependence of polyhydroxyalkanoic acid degradation in *Hydrogenophaga pseudoflava*. *J Biol Chem* **274**, 37800-37808.

Abstract: The first order intracellular degradation of various polyhydroxyalkanoic acid (PHA) inclusions in *Hydrogenophaga pseudoflava* cells was investigated by analyzing the compositional and microstructural changes of the PHA using gas chromatography, ¹³C NMR spectroscopy, and differential scanning calorimetry. Two types of PHA, copolymers and blend-type polymers, were separately accumulated in cells for comparison. The constituent monomers were 3-hydroxybutyric acid (3HB), 4-hydroxybutyric acid (4HB), and 3-hydroxyvaleric acid (3HV). It was found that the 3HB-4HB copolymer was degraded only when the polymer contained a minimal level of 3HB units. With the cells containing a 3HB/4HB blend-type polymer, only poly(3HB) was degraded, whereas poly(4HB) was not degraded, indicating the totally inactive nature of the intracellular depolymerase against poly(4HB). On the basis of the magnitude of the first order degradation rate constants, the relative substrate specificity of the depolymerase toward the constituting monomer units was determined to decrease in the order 3HB > 3HV > 4HB. ¹³C NMR resonances of the tetrad, triad, and dyad sequences were analyzed for the samples isolated before and after degradation experiments. The results showed that the intracellular degradation depended on the local monomer sequence of the copolymers. The relative substrate specificity of the depolymerase determined from the NMR local sequence analysis agreed well with that obtained from the kinetics analysis. It is suggested that, without isolation and purification of the intracellular PHA depolymerase and "native" PHA

substrates, the relative specificity of the enzyme as well as the microstructural heterogeneity of the PHA could be determined by measuring in situ the first order degradation rate constants of the PHA in cells.

Zhao C., Yao J., Masuda H., Kishore R., and Asakura T. (2003) Structural characterization and artificial fiber formation of Bombyx mori silk fibroin in hexafluoro-iso-propanol solvent system. *Biopolymers* **69**, 253-259.

Abstract: High-resolution solution (¹³C)-NMR and CD studies of Bombyx mori silk fibroin revealed the presence of an ordered secondary structure 3(10)-helix, in hexafluoro-iso-propanol (HFIP). The solid-state structure of the silk fibroin film prepared by drying it gently from the HFIP solution still keep the structure, 3(10)-helix, which was studied with high-resolution solid state (¹³C)-NMR. The structural transition from the 3(10)-helix to silk II structure, heterogeneous structure including antiparallel beta-sheet, occurred during the artificial spinning from the HFIP solution. The wide-angle x-ray diffraction and differential scanning calorimetry thermograms of the artificial spinning fiber after postspinning treatments were observed together with the stress-strain curves. The results emphasize that the molecular structures, controlled morphology, and mechanical properties of the protein-based synthetic polymers can be modulated for enhancing biocompatibility.

Zhou Y., Jiang K., Song Q. and Liu S. (2007) Thermo-induced formation of unimolecular and multimolecular micelles from novel double hydrophilic multiblock copolymers of n,n-dimethylacrylamide and N-isopropylacrylamide. *Langmuir* **23**, 13076-13084.

Abstract: Two novel double hydrophilic multiblock copolymers of N,N-dimethylacrylamide and N-isopropylacrylamide, m-PDMAp-PNIPAMq, with varying degrees of polymerization (DPs) for PDMA and PNIPAM sequences (p and q) were synthesized via consecutive reversible addition-fragmentation chain transfer (RAFT) polymerizations using polytrithiocarbonate (1) as the chain transfer agent (Scheme 1), where PDMA is poly(N,N-dimethylacrylamide) and PNIPAM is poly(N-isopropylacrylamide). The DPs of PDMA and PNIPAM sequences were determined by ¹H NMR, and the block numbers, i.e., number of PDMAp-PNIPAMq sequences (n), were obtained by comparing the molecular weights of multiblock copolymers to that of cleaved products as determined by gel permeation chromatography (GPC). m-PDMA42-PNIPAM37 and m-PDMA105-PNIPAM106 multiblock copolymers possess number-average molecular weights (M_n) of 4.62 x 10⁴ and 9.53 x 10⁴, respectively, and the polydispersities (M_w/M_n) are typically around 1.5. Block numbers of the obtained multiblock copolymers are ca. 4, which are considerably lower than the numbers of trithiocarbonate moieties per chain of 1 (approximately 20) and m-PDMAp precursors (approximately 6-7). PDMA homopolymer is water soluble to 100 degrees C, while PNIPAM has been well known to exhibit a lower critical solution temperature (LCST) at ca. 32 degrees C. In aqueous solution, m-PDMA42-PNIPAM37 and m-PDMA105-PNIPAM106 multiblock copolymers molecularly dissolve at room temperature, and their thermo-induced collapse and aggregation properties were characterized in detail by a combination of optical transmittance, fluorescence probe measurements, laser light scattering (LLS), and micro-differential scanning calorimetry (micro-DSC). It was found that chain lengths of PDMA and PNIPAM sequences exert dramatic effects on their aggregation behavior. m-PDMA105-PNIPAM106 multiblock copolymer behaves as protein-like polymers and exhibits intramolecular collapse upon heating, forming unimolecular flower-like micelles above the thermal phase transition temperature. On the other hand, m-PDMA42-PNIPAM37 multiblock copolymer exhibits collapse and intermolecular aggregation, forming associated multimolecular micelles at elevated temperatures. The intriguing aggregation behavior of this novel type of double hydrophilic multiblock copolymers argues well for their potential applications in many fields such as biomaterials and biomedicines.