# Characterisation of a novel self-association of an alternating copolymer into nanotubes in solution.

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## ABSTRACT

The characterisation of the association of an alternating copolymer was performed using theoretical methods (quantum mechanics and molecular mechanics) and experimental methods (cryo-Transmission Electron Microscopy, Neutron Reflectivity and Neutron Scattering). The most stable conformation obtained for the self-association at pH 7 using theoretical methods is a tubular structure in which eight SMA molecules make one twist of a helix. The tubes can grow in length by continued regular stacking of benzene rings. The nanotubes have inner and outer diameters of about 28 and 41 Å respectively. The hydrophobic groups are mainly located inside the tube and the hydrophilic groups are mainly on the exterior surface of the tube. They can also associate with themselves creating planes of aligned tubes, which can stack upon each other. The association of alternated copolymer into nanotubes has not been recognized before to the best of our knowledge(1).

The association of SMA octamers into a tubular structure at pH7 was confirmed experimentally by cryo-TEM and the nanotubes observed were several micrometers long. The shape as well as the inner and outer diameter of the nanotubes were also characterised by neutron scattering and the conformation at the air-water interface by neutron reflectivity.

***Keywords***: alternating copolymer, self-assembly, quantum mechanics, cryo-Transmission Electron Microscopy, Neutron Scattering.

## INTRODUCTION

Self-assembly is a very efficient method to obtain well defined and often defect-free nano-architectures. The association and variety of shapes and properties of block copolymers have been extensively studied. Applications of those associations range from foam stability to drug delivery. In contrast, the associations of alternating copolymers have been rarely studied. The present paper investigates the association of a specific alternating copolymer, poly(styrene-alt-maleic anhydride) (SMA), both numerically and experimentally.

Poly(styrene-alt maleic anhydride) is an alternating copolymer used in the pulp and paper industry as a surface sizing agent to enhance the printing. SMA is composed of alternating hydrophobic and hydrophilic group and its chemical structure is pH dependent; the different ionization states are shown in figure 1. The association of the SMA chains has previously been observed at neutral pH by Dynamic Light Scattering(2) over a wide range of molecular weights, with hydrodynamic radius in the order of microns. We chose a theoretical approach to characterize precisely the association of SMA in solution and to explain the pH dependence of SMA conformations.

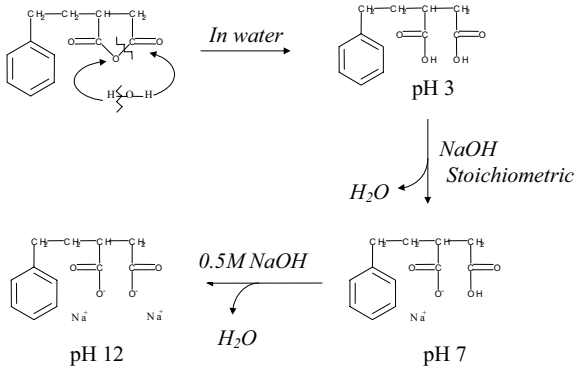



Figure 1: pH dependence of the molecular structure of poly(styrene-alt-maleic anhydride).

## 1 MONOMER CONFORMATIONS

Two methods of optimisation have been combined to obtain the ground state configuration of monomers at different pH values: the Tree Branch method(3) and a series of scans in energy(4) using the molecular modelling softwares Gaussian 98W(5) and Hyperchem(6). The calculations performed in this study are gas phase calculations and the difference in pH will be modelled using the different degrees of ionization of the polymer in solution (Fig. 1) The configurations obtained for the monomer at three different pH values are shown in figure 2. The main difference between the configurations occurs at pH 7 where the presence of a hydrogen bond stiffens the conformation of the molecule and as a result, the orientations of the binding sites for a second monomer are very different for pH 7 from those at pH 3 or 12. This hydrogen bond is very strong (1.68 Å), compared to a typical hydrogen bond (1.80 Å for water) and therefore is expected to be present in aqueous solution.

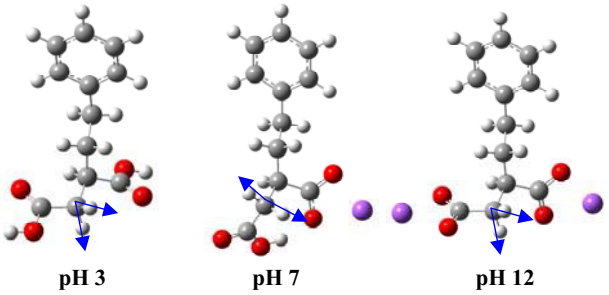



Figure 2: Optimised conformation of styrene maleic anhydride at 3 different pH values at the RHF/6-31G** level of theory. The orientations of the binding sites (⟶) at pH 7 are very different from the orientations of the binding sites at pH 3 or 12.

## 2 DIMER CONFORMATIONS

The dimer structure of SMA possesses two chiral centres and therefore all the structures need to be investigated. For the dimer conformation, four structures will be optimised: the RR, the RS, the SR and the SS conformations. The structures were optimised at the PM3 level of theory using series of scans in energy. These structures were reoptimised at the RHF/6-31G**.

The structures of the dimers obtained at pH 3 and pH 12 show a 90 degrees angle between the first monomer and the second (Fig. 3). The structures obtained at pH7 are very linear compared to pH 3 and 12. In addition the hydrogen bond observed in the monomer conformation is still present in the dimer structures (Fig. 3).

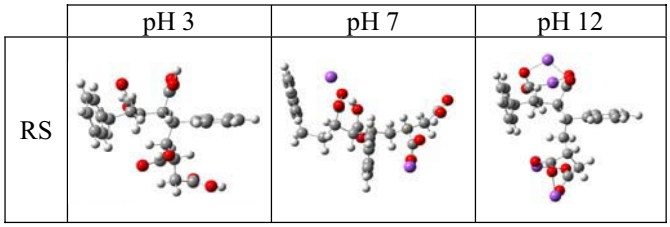



Figure 3: Optimised structure of dimers of SMA of RS chirality at pH 3, 7 and 12.

## 3 QUADRIMER CONFORMATIONS

The study of the quadrimer conformations at different pH values shows that the polymer at pH 7 is linear, unlike at pH 3 and at pH13 (Fig. 4). The linearity arises from the stiffening of the molecule by the internal H-bond observed in the monomer and dimer conformation. This conformation does not depend on the chirality of the chain[7].

In addition the orientation of the benzene groups at pH7 are very similar for all the different possible chiralities of the chain. The linearity of the conformation and the similar orientation of the benzene groups therefore allow strong association between the polymer chains.

At low or high pH no association was observed because the conformation is an irregular helix. The irregularity of the helix at pH 3 and 13 is due to the chirality dependence of the conformation at low and high pH[7]. The study of the quadrimers, pentamers and hexamers showed that the conformation of SMA at pH7 is repetitive from the trimer[8].

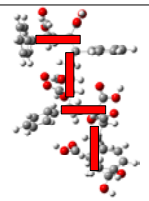
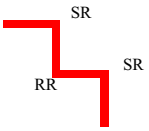
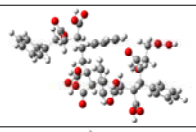
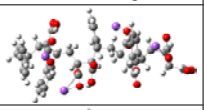
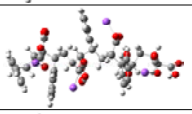
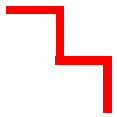
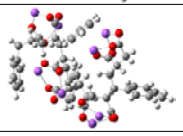
| pH | Chirality | Optimised structure | Backbone |
|---|---|---|---|
| pH 3 | SR RR SR |  |   |
| | SR SR SR |  |  |
| pH 7 | SR RR SR |  |  |
| | SR SR SR |  |  |
| pH 12 | SR RR SR |  |  |
| | SR SR SR |  |  |

Figure 4: Optimised structure and schematic backbone representation of quadrimers of SMA of different chirality at pH 3, 7 and 12. At pH 7, the structures are linear, independent of the chirality of the chains.

## 4 ASSOCIATION AT PH 7

When two molecular chains at pH 7 associate, the angle between them is 90°, therefore by associating eight SMA molecules a tube can be formed. The front view of this tube is a square due to the 90° angle between two chains. As an example, the association of dodecamers was studied using molecular modelling and the most stable conformation was found to be a tubular conformation for which the inside of the tube is mainly hydrophobic, whereas the exterior is mainly hydrophilic (Fig. 5). The cavity of the tube was determined to be about 28 Å and the external diameter about 41 Å. The tubular structure is maintained by stacking interactions between the benzene groups of poly(styrene-maleic anhydride) and therefore this interaction, studied in the gas phase, is likely to be stable in water. This way of self-assembly in nanotubes has not been recognized before:

a recent review on organic nanotubes mentions four possible strategies for the molecular assembly of tubular materials[1], but the self-assembly of rigid alternating copolymers is not considered. The interactions occurring between the chains are hydrophobic interactions, protecting the benzene groups from contact with water.

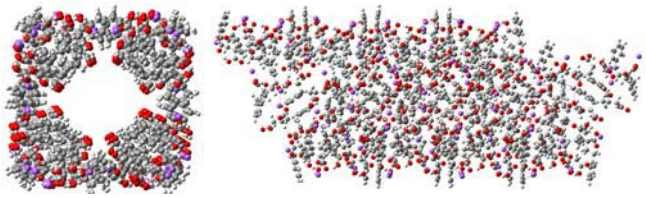


Figure 5: Front view and side view of the configuration of the tubular association of SMA dodecamers at pH 7 at the molecular mechanical level.

This association can grow in two directions: at the tube ends to increase the length (longitudinal growth) and between the tubes to increase the width (radial growth) (Fig. 6). In addition the association does not depend on the molecular weight nor on the polydispersity of the SMA chains; indeed small chains can easily associate with long chains (Fig. 6). The tubes can also associate with themselves creating planes of aligned tubes (Fig.6). The planes can then associate with an angle of 45° between the orientations of the tubes in the planes due to the orientation of the benzene groups with respect to the tube growth.

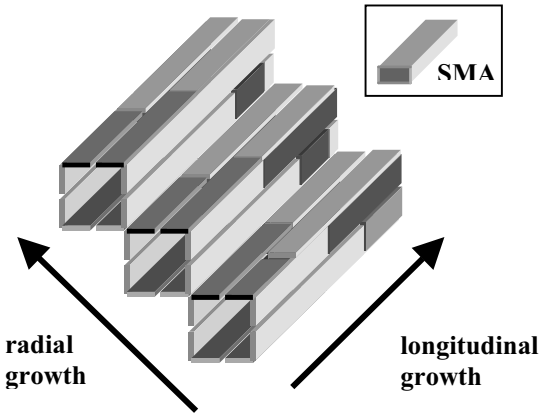



Figure 6: Schematic representation of the growth of the SMA association at pH 7 in the radial and longitudinal directions.

## 5 CRYO-TEM CHARACTERISATION

We performed experiments to observe the tubular structures in water by cryo-TEM. In these experiments, a drop of an aqueous solution of octamers of SMA (of molecular weight 1600) at a given pH was refrigerated in liquid nitrogen. The frozen sample was cut, and a replica of the top surface was obtained by first spraying a platinum-carbon mixture at 45° with respect to the surface and then by spraying carbon normal to the surface. In preparing samples for cryo-TEM, the surface often fractures at locations were discontinuities in structure occur. The results obtained with this method for pH 7 show very long lines with a spacing of about 50 Å, which closely corresponds to the diameter of the nanotubes calculated theoretically. These lines are organized in sheets, one on top of the other, with the lines of one sheet making an angle of 45° with the other sheet (Fig. 7). This angle is due to the stacking interaction between benzene groups, which make a 45° angle with the main axis of the tube. No regular structure was observed by cryo-TEM at pH 12.

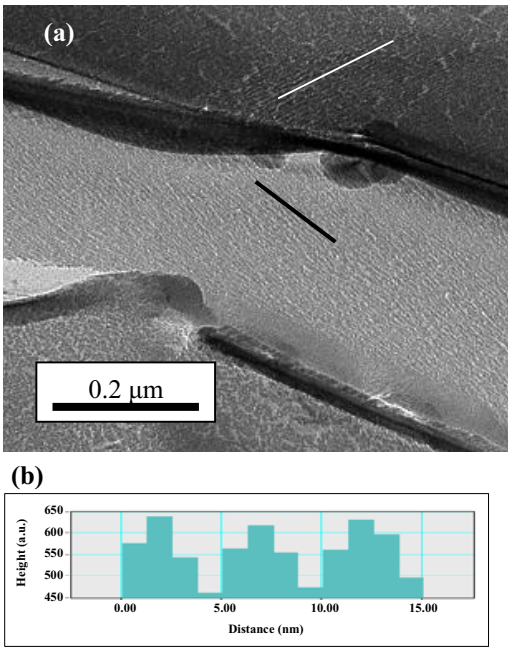



Figure 7: (a) Cryo-TEM picture of the association of SMA in solution 1% wt at pH 7. The lines represent the direction of the tubular association of SMA.
(b) Height profile of three lines of the cryo-TEM image, showing that the diameter of one tube is about 50 Å.

## 6 NEUTRON SCATTERING CHARACTERISATION

In order to fully characterise the association at the molecular level and the macromolecular properties influencing the structure of SMA at pH 7, a neutron scattering study has been performed at ILL (Grenoble, France).

The profiles obtained were fitted with a model using nanotubes interacting with a spherical potential. The fitted result for a 2% wt SMA solution at pH 7 (molecular weight 40,000) is shown in figure 8. The fitted inner and outer radii of the nanotube are 14 Å and 19 Å respectively, which closely correspond to the predicted radii. The profile at pH 7 can be compared to the profile at pH 12 where no structure factor was observed (Fig. 9).

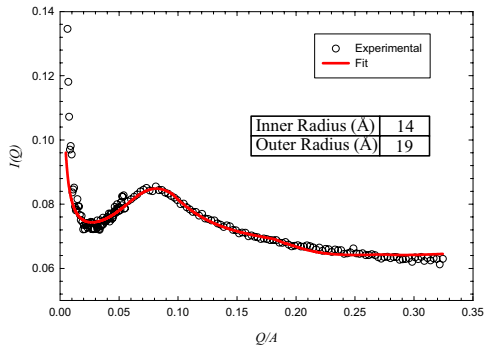



Figure 8: Neutron scattering profile and fitting curve of 2% wt SMA solution at pH 7.

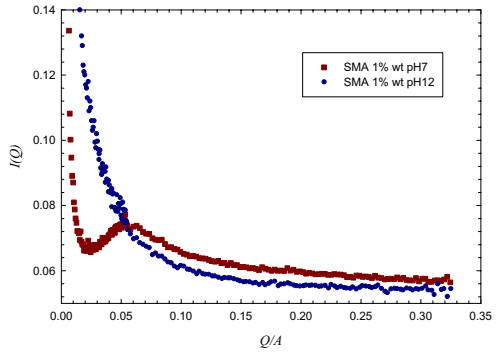



Figure 9: Neutron scattering profile of 1% wt SMA solution at pH 7 and pH 12.

## 7 NEUTRON REFECTIVITY

To understand the mechanism of association at pH 7 and the influence of the conformation of SMA at the air-water interface, neutron reflectivity experiments[9,10] were performed at NIST (Washington, USA). These experiments were performed with 1%wt solutions of the deuterated ethyl esters of poly(styrene-maleic anhydride), used in order to label the hydrophilic part of SMA.

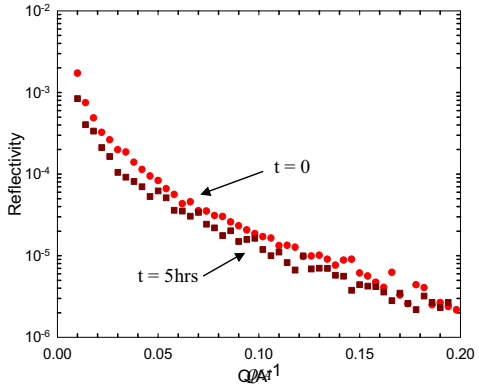



Figure 10: Neutron reflectivity profile of the ethyl ester of SMA, residing at an air-water interface at pH 7.

The results obtained show that a complete monolayer of SMA is formed at the air-water interface at pH 3 and 7, with a coverage of about 1.2 mg/m$^2$. At pH 13, the polymer is more soluble and forms an incomplete monolayer (coverage 0.9 mg/m$^2$). SMA adsorbs in a flat configuration, with the benzene groups sticking out in the air. The association does influence the conformation at the air-water interface at pH 7, as a 5 hr delay is observed in obtaining a stable signal (Fig. 10). (Such a delay was not observed at low or high pH). This delay is likely due to the slow establishment of an equilibrium between associated SMA molecules in solution and single SMA molecules at the air-water interface.

## CONCLUSION

The association of an alternating copolymer observed by DLS was characterized by theoretical and experimental methods. The association consists of eight SMA chains associated into a nanotube with an inner diameter of 28 Å and an outer diameter of 41 Å. The nanotubes can then associate to form a 2 dimensional structure, the planes obtained by self-association of the nanotubes can stack upon each other by hydrophobic interaction and form a 3 dimensional architecture. The association of alternated copolymer into nanotubes has not been recognized before.

The structure predicted by theoretical calculations was confirmed and observed by cryo-TEM and neutron scattering. In addition, an equilibrium was observed between associated SMA molecules in solution and single SMA molecules at the air-water interface by neutron reflectivity.

## ACKNOWLEDGMENTS

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