Introduction
The objective of this study is to develop thermo-responsive nano-constructs. The approach followed in the past to render nano-particles with the ability to respond to small temperature differentials, aimed at grafting thermo-responsive chains onto the surface of various nanoparticles [1] or blending them with a non-responsive matrix [2]. Expectedly, these nano-particles displayed a very limited ability to respond to temperature changes since a non-responsive component was part of the system. This contribution introduces totally thermo-responsive hollow nano-structures, comprising only poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) (PEO-PPO-PEO) triblocks [3]. The uniqueness of these novel nano-sized constructs stems from their ability to display a remarkable and reversible change in size (up to 1000 times by volume), within a narrow temperature interval. These supramolecular architectures are produced by cross-linking intramicellarly end-capped PEO-PPO-PEO dimethacrylates, while these amphiphilic triblocks are constrained to the specific spatial configuration dictated by their micellar organization.

Materials and Methods
(I) Pluronic F-127 dimethacrylate [4]. The PEO-PPO-PEO dimethacrylate derivatives (F127-DMA) were obtained by the reaction of the native OH-terminated PEO-PPO-PEO triblock with methacryloyl chloride. The functionalization of the triblock was demonstrated by 1H-NMR analysis and FTIR spectroscopy. Once F127-DMA formed micelles in aqueous medium, they were crosslinked intramicellarly by free radical polymerization, using ammonium persulfate, ferrous sulfate and L-ascorbic acid.
(II) Biodegradable NanoShells were obtained, by the ring opening polymerization of L-lactide, initiated by the terminal hydroxyl groups of F-127, followed by the incorporation of the methacrylate moieties.
(III) Dynamic Light Scattering. The average hydrodynamic radius of the microstructures present in the aqueous medium was measured by dynamic light scattering (HPPS, HPPS001, Malvern Instruments, U.K).
(IV) Transmission electron microscopy. Samples were lyophilized with liquid nitrogen and then re-dissolved in water prior to use and dried on the grid.

Results and Discussion
The cross-linking of the hydrophilic PEO shell, not only stabilized the micelles, resulting in extremely robust nano-constructs but rendered them also with a unique dimensional reverse thermo-responsive behavior. F127 triblocks appear as molecular unimers at low temperatures and they form a micelle, at a higher temperature. For example, at 15 °C, the size of F127 unimers is 6-7 nanometers, while its micelles attain a size of around 20 nanometers, at 40 °C. Once the temperature decreases below $c_m$, the micelles disassemble, reverting to their unimeric state. In fundamental contrast to the above, the affixed nano-sized constructs engineered decrease in size markedly when going from a lower temperature to a higher one, in a sharp and essentially reversible manner. Spherical Nano-Shells formed at 50 °C exhibited a diameter of around 200 nanometers at 15°C, while displaying a markedly smaller size (approximately 30 nanometers in diameter) at 40°C, as shown in the figure below.

Since the shape and size of the micelles depend on the temperature, Nano-Shells having various geometries, were "sculptured" by performing the cross-linking reaction at different temperatures. Tubular nanoshells were formed by crosslinking rod-like micelles at 80°C. Their size shifted from 3000 nanometer at 15°C, to around 300 nanometers at 40°C (as hown in the figure below).

Work was also devoted to impart to these NanoShells additional features, such as pH-responsiveness, and biodegradability.

References