

## SUPPORTING INFORMATION I

### Synthesis of 4-(Hexadecyloxy)benzaldehyde

A mixture of 7.5 g (61.4 mmol) of 4-hydroxybenzaldehyde and 10 g (30.7 mmol) of cesium carbonate in anhydrous methanol (300 mL) was refluxed for 1 hr. After removal of the solvent by rotary evaporation, the dry cesium salt was dissolved in DMF (200 mL), hexadecyl iodide (21.6 g, 91.4 mmol) was added and the mixture stirred for 48 hr at 80 °C. The solvent was removed by vacuum distillation and the remaining residue was dissolved in chloroform and filtered. The solvent was removed by rotary evaporation and the crude product was recrystallized from anhydrous acetone. The yield was 11 g, 50%; mp 45 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.9 (t, 3H, -CH<sub>3</sub>), 1.4 (m, 26H, -CH<sub>2</sub>-), 1.8 (m, 2H, β-CH<sub>2</sub>), 4.0 (t, 2H, α-CH<sub>2</sub>), 6.9 (d, 2H Ar-H), 7.8 (d, 2H, Ar-H), 9.9 (s, 1H, aldehyde-H); IR (chloroform cast film) cm<sup>-1</sup> 2919 (aliphatic C-H stretch), 1689 (carbonyl stretch).

### Synthesis of 4-(Hexadecyloxy)benzaldehyde Hydrazone

4-(Hexadecyloxy)benzaldehyde (6.5 g, 18 mmol) was dissolved in 100 mL of anhydrous diethyl ether and the solution was slowly dropped into 150 mL of anhydrous diethyl ether containing 1.5 mL (47 mmol) of hydrazine at 4°C. In 3-5 min, a white precipitate appeared in the solution and the reaction mixture was stirred at 4°C for 4 hr. The white precipitate was filtered and washed with cold anhydrous diethyl ether. The yield was 5.2 g, 65%; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.9 (t, 3H, -CH<sub>3</sub>), 1.4 (m, 26H, -CH<sub>2</sub>-), 1.8 (m, 2H, β-CH<sub>2</sub>), 4.0 (t, 2H, α-CH<sub>2</sub>), 6.9 (d, 2H Ar-H), 7.5 (d, 2H, Ar-H), 7.7 (s, 1H, imine-H); IR (KBr film) cm<sup>-1</sup> 3354 (N-H), 2919 (C-H).

### Synthesis of 4-(Hexadecyloxy)phenyldiazomethane

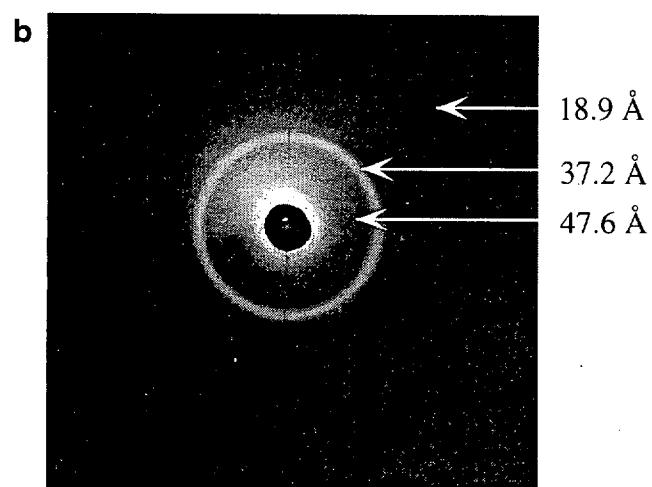
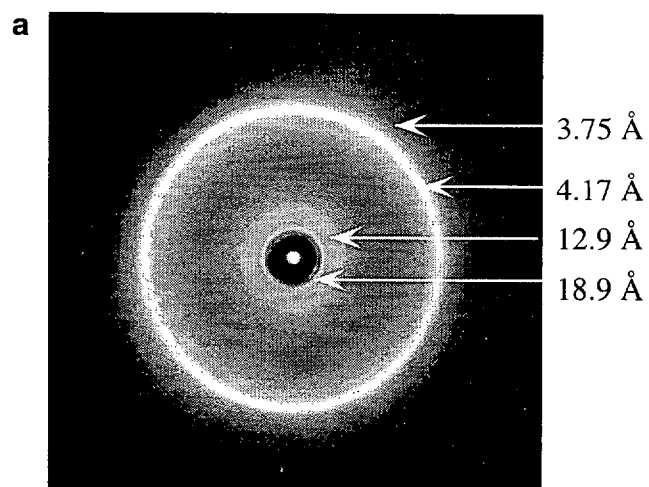
4-(Hexadecyloxy)benzaldehyde hydrazone (1g, 2.25 mmol) was added to 50 mL of benzene and stirred at 40 °C until dissolution. HgO (1.3 g, 6 mmol) and 200 μL of saturated KOH/EtOH solution were added and the mixture was stirred at room temperature for 20 min. The

reaction mixture was filtered twice and the red-purple benzene solution containing the diazo compound was washed four times with 100 mL of water. This solution showed a strong absorption band at  $\lambda_{\max}=500$  nm and was used directly for the reaction with **PLGA-X**. Titration with benzoic acid in benzene solution gave approximately 35% reaction yield.

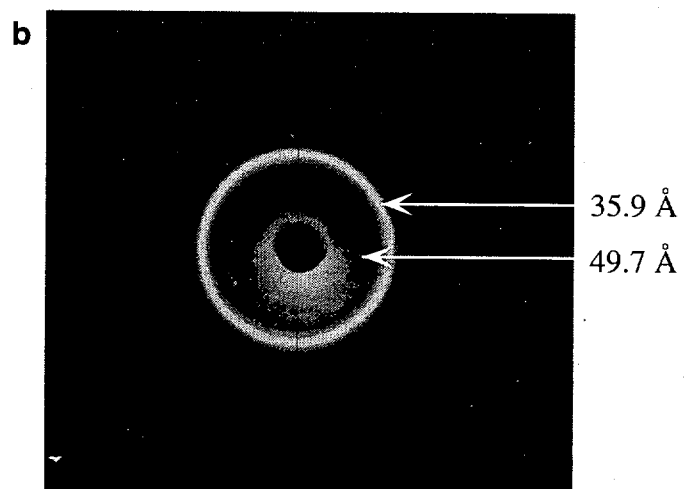
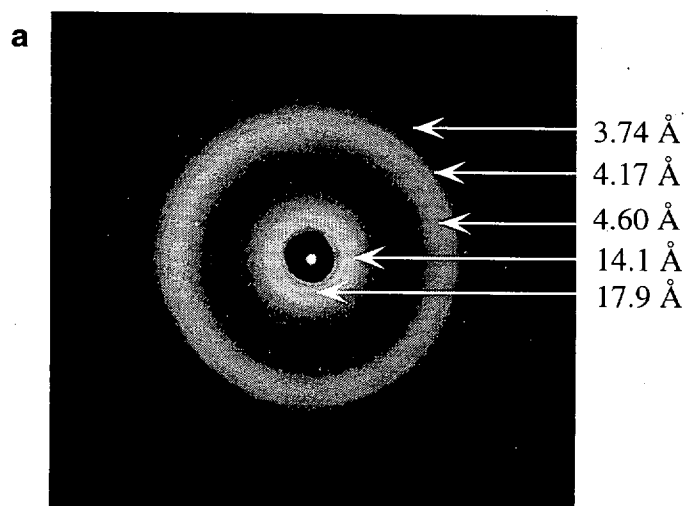
**Synthesis of Monodisperse Derivatives of Poly( $\gamma$ -4-(hexadecyloxy)benzyl  $\alpha$ ,L-glutamate) (PHBG-4)**

**PLGA-4** (sodium salt, 70 mg, 0.4 mmol repeating units) was dissolved in 15 mL of water and acidified to pH 1.4 with dilute aqueous HCl. The precipitated polymer was purified by ultrafiltration (Amicon, MWCO = 3000) and dried under vacuum overnight. The polymer was dissolved in 80 mL of DMSO and 50 mL of 4-(hexadecyloxy)phenyl diazomethane (approximately 0.8 mmol) solution was added. The reaction mixture was stirred at room temperature for 48 hr in the dark. DMSO was removed by vacuum distillation and the remaining solid was dissolved in 30 mL of dichloromethane, and centrifuged at 4 °C for 30 min. The clear solution which was present in the lower part of the centrifuge tube was carefully withdrawn by Pasteur pipette and added to 10 fold excess dioxane and stored at 4 °C overnight. The white precipitate was isolated by centrifugation, washed with cold dioxane and dried. The yield was 50%. The same procedure was used to produce other PHBGs with comparable reaction yields.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  0.9 (3H, - $\text{CH}_3$ ), 1.4 (26H, - $\text{CH}_2$ -), 1.8 (2H,  $\beta$ - $\text{CH}_2$  of hexadecyl group), 2.1-2.8 (4H,  $\beta$ - and  $\gamma$ - $\text{CH}_2$  of glutamate), 3.8 (2H, - $\text{OCH}_2$ -), 4.0 (1H,  $\alpha$ -CH of glutamate), 4.7-5.1 (2H, benzylic  $\text{CH}_2$ ), 6.8 (2H Ar-H), 7.2 (2H, Ar-H), 8.4 (1H, amide H).

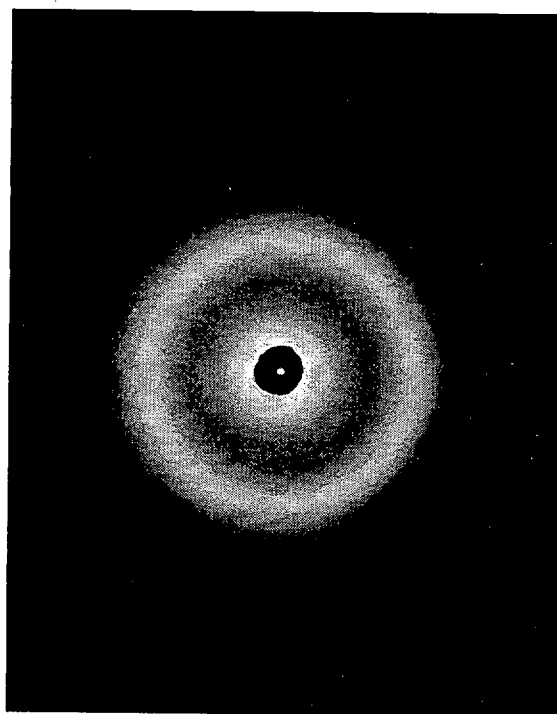
SUPPORTING INFORMATION II



X-ray diffraction patterns of **PHBG-4** recorded at 25°C with camera distances of 5.01 cm (a) and 29.01 cm (b).



X-ray diffraction patterns of **PHBG-4** recorded at 70°C with camera distances of 5.01 cm (a) and 29.01 cm (b).



X-ray diffraction pattern of **PHBG-4** recorded at 110°C with camera distance of 5.01 cm.